ORIGINAL

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
FORT WORTH DIVISION

GALDERMA LABORATORIES, L.P. and GALDERMA S.A.,	§	
Plaintiffs,	§	3-06CV1176-N
v.	§	**CAUSE NO.** _____
ACTAVIS MID-ATLANTIC, L.L.C.,	§	
Defendant	§	**Jury Trial Requested**

ORIGINAL COMPLAINT

Plaintiffs, GALDERMA LABORATORIES, L.P. ("Galderma L.P.") and GALDERMA S.A. ("Galderma S.A."), file this Original Complaint against Defendant, ACTAVIS MID-ATLANTIC, L.L.C. ("Actavis"), and state:

INTRODUCTION

1. This is a civil action for patent infringement in violation of the United States Patent Act, 35 U.S.C. § 271, et seq.

2. This suit stems from Actavis' filing of an Abbreviated New Drug Application (the "ANDA") with the United States Food and Drug Administration (the "FDA") pursuant to 21 U.S.C. § 355.

PARTIES

3. Galderma L.P. is a Texas limited partnership, with its principal business address at 14501 N. Freeway, Fort Worth, Texas 76177. Galderma L.P. is the beneficial holder of rights to market Clobex (clobetasol propionate) Lotion, 0.05% ("Clobex Lotion") under FDA approval

of New Drug Application No. 021535 (the "FDA Approval"). Galderma L.P. has an exclusive license from Galderma S.A. to distribute Clobex in the United States.

4. Galderma S.A. is a Swiss corporation, with its principal business address at World Trade Center, Avenue de Gratta-Paille, Case postale 453, CH-Lausanne 30, Switzerland. Galderma S.A. owns United States Patent No. 6,106,848 (the "'848 Patent").

5. Actavis (formerly known as Alpharma USPD, Inc.) is a Delaware limited liability company, with its principal place of business at 200 Elmora Ave., Elizabeth, New Jersey 07207. Actavis may be served with process by and through its registered agent for service of process United Corporation Services, Inc., 874 Walker Road, Suite C, Dover, Delaware 19904.

JURISDICTION AND VENUE

6. This is a complaint for patent infringement and for declaratory judgment of patent infringement. This Court has jurisdiction over the subject matter of the claims asserted pursuant to 28 U.S.C. §§ 1331 and 1338(c), as well as 28 U.S.C. §§ 2201 and 2202. Venue in this Court is proper under 28 U.S.C. §§ 1391 and 1400(b).

7. This Court has personal jurisdiction over Actavis in that Actavis sells products for distribution throughout the United States and, on information and belief, regularly conducts business in the State of Texas. Actavis also filed the ANDA for the infringing product and issued a certification under 21 U.S.C. § 355(j)(2)(B) (the "Paragraph IV Certification") – the acts which give rise to the instant litigation – with knowledge that Galderma L.P. would be injured by such actions in this district, and delivered its Paragraph IV Certification to Galderma L.P. in this district. Moreover, on information and belief, Actavis intends to sell the infringing product in or

for distribution to this district upon approval by the FDA. Actavis has thus purposefully targeted its conduct to cause harm in the State of Texas and this district.

8. Venue is appropriate in this district because the claims asserted herein arise out of an act of patent infringement (i.e. Actavis's filing of the ANDA and issuance of the Paragaph IV certification) purposefully targeting a resident of this district (i.e. Galderma L.P.). Further, because 21 U.S.C. § 355(j)(2)(C)(i)(II) establishes this district as the only venue in which Actavis could file suit seeking a declaration of non-infringement in connection with the ANDA, venue is proper in this district for this action.

BACKGROUND FACTS

A. The '848 Patent

9. On September 22, 1997, Isabelle Preuilh and Nathalie Willcox (inventors) and Centre International de Recherches Dermatologiques (assignee) filed an application with the United States Patent and Trademark Office ("USPTO"), namely, United States Patent Application Serial No. 08/935,054 (the "'054 Application") entitled "Topically Applicable O/W Emulsions Having High Glycol Content and At Least One Biologically Active Agent." On August 22, 2000, based on the '054 Application, the USPTO issued the '848 Patent. A copy of the '848 Patent is attached as Exhibit "A."

10. The '848 Patent is directed to certain emulsions, which are described generally as:

> Stable, topically applicable oil-in-water bioaffecting emulsions having intermediate viscosity, characteristically ranging from 3 to 10 Pa·s, comprise (a) from 30% to 50% by weight of at least one pro-penetrating glycol, (b) at least one emulsifying agent, advantageously an anionic amphiphilic polymer, and (c) at least one biologically active agent, for example an active agent that modulates skin differentiation and/or proliferation and/or pigmentation, an anti-inflammatory, an antibacterial, an antifungal, etc.

'848 Patent at Abstract, p. 1.

11. The '848 Patent is valid, enforceable, and has not expired.

12. Isabelle Preuilh and Nathalie Willcox assigned their rights to and interest in the '054 Application and the '848 Patent to Centre International de Recherches Dermatologiques. Centre International de Recherches Dermatologiques assigned the '848 Patent to Galderma S.A.

13. On July 24, 2003, Galderma L.P. obtained the FDA Approval to market Clobex Lotion. The '848 Patent is listed in the FDA's Approved Drug Products list (the "Orange Book") as reading on Clobex Lotion.

14. On August 18, 2003, Galderma S.A. granted Galderma L.P. the exclusive right to distribute Clobex Lotion in the United States.

B. Actavis's Infringement

15. Upon information and belief, Actavis is in the business of developing, manufacturing, and marketing generic pharmaceutical products.

16. On or about March 24, 2006, Actavis filed ANDA No. 78-223 for Clobetasol Propionate Lotion, 0.05% (the "Accused Product"). Pursuant to the ANDA, Actavis seeks permission from the FDA to market and sell the Accused Product in the United States.

17. On or about May 22, 2006, Actavis mailed a letter (the "Certification Letter") to Galderma L.P. in Fort Worth, Texas, and to Galderma S.A. in Switzerland. A copy of the Certification Letter is attached as Exhibit "B". Through the Certification Letter, Actavis first notified Plaintiffs that Actavis had filed the ANDA with the FDA relating to the Accused Product.

18. In the Certification Letter, Actavis contends that "the claims of [the '848 Patent] are invalid and/or will not be infringed by the commercial manufacture, use or sale of the [Accused Product]." Certification Letter at p. 2. Plaintiffs dispute this contention.

19. Plaintiffs are filing this Original Complaint within forty-five (45) days of receipt of the Certification Letter.

COUNT I
(PATENT INFRINGEMENT)

20. Plaintiffs incorporate paragraphs 1 through 19 above by reference as if fully set forth herein.

21. 35 U.S.C. § 271(e)(2)(A) provides:

> It shall be an act of infringement to submit . . an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act [codified at 21 U.S.C. § 355(j)] or described in section [355(b)(2)] of such Act for a drug claimed in a patent or the use of which is claimed in a patent . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

22. The '848 Patent is valid, enforceable, and has not expired. Also, the Accused Product falls within the scope of the claims of the '848 Patent. As such, Actavis infringed the '848 Patent by filing the ANDA seeking permission to commercially manufacture, use, or sell the Accused Product prior to the expiration of the '848 Patent.

23. As a result of Actavis' infringement, Plaintiffs are entitled to a declaration that (a) the '848 Patent is valid and enforceable, and (b) the Accused Product infringes the '848 Patent if made, used, sold or offered for sale during the term of the '848 Patent.

24. As a result of Actavis' infringement, Plaintiffs are entitled to permanent injunctive relief, restraining and enjoining Actavis and all those in privity with or acting in

concert with Actavis from manufacturing, selling, or offering the Accused Product for sale during the term of the '848 Patent, or from otherwise infringing or inducing the infringement of the '848 Patent.

DEMAND FOR JURY TRIAL

Plaintiffs hereby demand trial by jury of all issues and claims alleged herein.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs hereby pray for the following relief:

(A) A declaration that the '848 Patent is valid and enforceable;

(B) A declaration, pursuant to 35 U.S.C. § 271(e), that Actavis has infringed one or more claims of the '848 Patent by filing the ANDA;

(C) A declaration, pursuant to 35 U.S.C. § 271(e)(4)(A), that the effective date of any approval of the ANDA is not to be earlier than the expiration date of the '848 Patent;

(D) A permanent injunction, pursuant to 35 U.S.C. §§ 271(e)(4)(B) and 283, enjoining Actavis and its officers, agents, servants, employees, privies, and others acting for, on behalf of, or in concert with any of them from manufacturing, selling, or offering the Accused Product for sale, or from otherwise infringing or inducing the infringement of the '848 Patent;

(E) An award to Plaintiffs, pursuant to 35 U.S.C. § 271(e)(4)(C), of damages and other monetary relief, including enhanced damages, as a result of Actavis' infringement, if there has been any commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of the Accused Product prior to expiration of the '848 Patent;

(F) An award, pursuant to 35 U.S.C. §§ 271(e)(4) and 285, declaring this case exceptional and granting Plaintiffs their costs and attorneys fees in pursuing this case; and

(G) Such other and further relief as this Court may deem just and proper.

Respectfully submitted,

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EXHIBIT "A"

United States Patent [19]

Preuilh et al.

[11] **6,100,848**

[45] **Date of Patent: *Aug. 22, 2000**

[54] **TOPICALLY APPLICABLE O/W EMULSIONS HAVING HIGH GLYCOL CONTENT AND AT LEAST ONE BIOLOGICALLY ACTIVE AGENT**

[75] Inventors: **Isabelle Preuilh**, Le Canet; **Nathalie Willcox**, Le Rouret, both of France

[73] Assignee: **Centre International de Recherches Dermatologiques**, Valbonne, France

[*] Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

[21] Appl. No.: **08/935,054**

[22] Filed: **Sep. 22, 1997**

[30] **Foreign Application Priority Data**

Sep. 20, 1996 [FR] France 96 11510

[51] **Int. Cl.**[7] **A61K 9/07**; A61K 47/10; A61K 47/14; A61K 47/30

[52] **U.S. Cl.** **424/401**; 424/59; 424/62; 424/63; 424/65; 424/70.1; 424/70.6; 424/70.8; 424/70.9; 424/70.11; 424/70.16; 424/70.21; 424/70.22; 424/73; 523/105; 523/122; 514/818; 514/852; 514/859; 514/864; 514/875; 514/880; 514/882; 514/886; 514/887; 514/937; 514/938; 514/939; 514/940; 514/941

[58] **Field of Search** 523/102–105, 523/122; 524/386; 510/158–160; 574/817, 818, 825, 828, 844–848, 852, 855, 865, 871, 873–875, 880–882, 886, 887, 928, 937–941, 947; 424/405, 401, 59

[56] **References Cited**

FOREIGN PATENT DOCUMENTS

0268164	5/1988	European Pat. Off. .
0279641	8/1988	European Pat. Off. .
0347225	12/1989	European Pat. Off. .
2646435	4/1978	Germany .
94/17830	8/1994	WIPO .

Primary Examiner—Neil S. Levy
Attorney, Agent, or Firm—Burns, Doane, Swecker & Mathis, L.L.P.

[57] **ABSTRACT**

Stable, topically applicable oil-in-water bioaffecting emulsions having intermediate viscosity, characteristically ranging from 3 to 10 Pa·s, comprise (a) from 30% to 50% by weight of at least one pro-penetrating glycol, (b) at least one emulsifying agent, advantageously an anionic amphiphilic polymer, and (c) at least one biologically active agent, for example an active agent that modulates skin differentiation and/or proliferation and/or pigmentation, an anti-inflammatory, an antibacterial, an antifungal, etc.

20 Claims, No Drawings

TOPICALLY APPLICABLE O/W EMULSIONS HAVING HIGH GLYCOL CONTENT AND AT LEAST ONE BIOLOGICALLY ACTIVE AGENT

This application claims benefit of priority under 35 U.S.C. §119 to French Application No. 96-11510, filed on Sep. 20, 1996.

BACKGROUND OF THE INVENTION

1. Technical Field of the Invention

The present invention relates to novel topically applicable oil-in-water (O/W) emulsions comprising a high content of at least one pro-penetrating glycol, an appropriate emulsifying system and at least one biologically active agent.

2. Description of the Prior Art

Currently marketed are numerous topical compositions comprising an active agent and a high content of glycol, the latter promoting the penetration of the biologically active agent into the skin. Given the high content of pro-penetrating glycol, these compositions are formulated as emulsions having a high content of fatty phase which are also commonly designated "lipocreams," as anhydrous compositions which are deemed "ointments," as fluid compositions having a high content of volatile solvents, such as ethanol or isopropanol, which are destined for application to the scalp, i.e., "hair lotions," or, alternatively, as viscous O/W emulsions which are also designated "O/W creams."

O/W creams comprising a corticoid and including a high percentage of propylene glycol (47.5%), which are marketed under the trademark TEMOVATE® by GLAXO, are known to this art. Indeed, the stabilization of a formulation comprising such a percentage of glycol necessitates incorporating, in the emulsion, emulsifying and stabilizing agents of the glyceryl stearate or PEG 100 stearate type or, alternatively, stabilizing agents or consistency factors of the white wax or ketostearyl alcohol type which form a viscous cream, namely, whose viscosity is greater than 10 Pa·s (10,000 centipoises, measured with a Brookfield apparatus model LVDV II+paddle No. 4, at a speed of 30 revolutions/min for 30 seconds and at a temperature of 25° C.±3° C.).

To facilitate the application of topical compositions comprising a high percentage of glycol, it would be desirable to provide novel formulations of the O/W emulsion type, whose viscosity would be intermediate between the hair lotions which are too fluid and the use of which is too limited, and the O/W creams which are too viscous and which have a fatty and sticky characteristic, while preserving the propenetrating properties of the glycol.

SUMMARY OF THE INVENTION

Accordingly, a major object of the present invention is the provision of novel topically applicable oil-in-water (O/W) emulsions, comprising from 30% to 50% by weight relative to the total weight of the composition of at least one glycol, an appropriate emulsifying system and at least one biologically active agent.

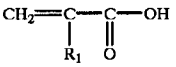
DETAILED DESCRIPTION OF BEST MODE AND SPECIFIC/PREFERRED EMBODIMENTS OF THE INVENTION

More particularly according to the present invention, by "fluid emulsion" is advantageously intended an emulsion whose viscosity ranges from 3 to 10 Pa·s (3,000 to 10,000 centipoises), a viscosity measured with a Brookfield apparatus model LVDV II+paddle No. 4, at a speed of 30 revolutions/min for 30 seconds and at a temperature of 25° C.±3° C.

Advantageously, a stable emulsion is provided according to the invention by selecting, as an appropriate emulsifying system, at least one polymeric emulsifier. The polymeric emulsifiers are in particular described by CLYMANS & BRAND in "Cosmetics and Toiletries" (manufacture worldwide, 1995, 119–125).

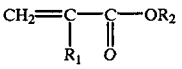
These are, in particular, anionic amphiphilic polymers, more especially those comprising at least one hydrophilic recurring structural unit of the unsaturated olefin carboxylic acid type, and at least one hydrophobic recurring structural unit of the C_{10}–C_{30} alkyl ester type.

According to the invention, acrylic structural units are those of the formula:



in which R_1 is H, CH_3 or C_2H_5, namely, acrylic acid, methacrylic acid or ethacrylic acid structural units.

Alkyl acrylate structural units are those of the formula:



in which R_1 is H, CH_3 or C_2H_5, namely, acrylate, methacrylate or ethacrylate units, and R_2 is a C_{10}–C_{30}, preferably C_{12}–C_{22}, alkyl radical.

Exemplary acrylates according to the invention include lauryl acrylate, stearyl acrylate, decyl acrylate, isodecyl acrylate, dodecyl acrylate and the corresponding methacrylates, lauryl methacrylate, stearyl methacrylate, decyl methacrylate, isodecyl methacrylate and dodecyl methacrylate.

Preferably, the above anionic amphiphilic polymers are crosslinked using a crosslinking polymerizable comonomer containing a CH_2=C< group with at least one other polymerizable group whose sites of unsaturation are not conjugated relative to each other.

Exemplary such crosslinking polymerizable comonomers preferably include polyallyl ethers such as, in particular, polyallylsucrose and polyallylpentaerythritol.

Crosslinked polymers of this type are well known to this art; they are, in particular, described in U.S. Pat. Nos. 3,915,921 and 4,509,949.

According to the invention, anionic amphiphilic polymers are preferred which comprise 95% to 60% by weight of acrylic recurring structural units, 4% to 40% by weight of acrylate recurring structural units and 0.1% to 6% by weight of crosslinking monomer, or (ii) which comprise 98% to 96% by weight of acrylic recurring structural units, 1% to 4% by weight of acrylate recurring structural units and 0.1% to 0.6% by weight of crosslinking monomer.

Among said crosslinked polymers indicated above, those marketed by GOODRICH under the trademarks PEMULEN TR1, PEMULEN TR2, CARBOPOL 1342 and CARBOPOL 1382 are most particularly preferred according to the present invention.

The compositions according to the invention advantageously comprise up to 1 by weight of appropriate emulsifying system, preferably from 0.2% to 0.4% by weight relative to the total weight of the composition.

The pro-penetrating glycol is advantageously selected from among propylene glycol, dipropylene glycol, propylene glycol dipelargonate, lauroglycol or ethoxydiglycol.

Preferably, the compositions according to the invention comprise from 40% to 50% by weight of pro-penetrating glycol.

Exemplary active agents according to this invention include the agents modulating skin differentiation and/or proliferation and/or pigmentation such as retinoic acid and isomers thereof, retinol and esters thereof, retinal, retinoids, in particular those described in FR-2,570,377, EP-199,636, EP-325,540, EP-402,072, vitamin D and derivatives thereof, estrogens such as estradiol, kojic acid or hydroquinone; antibacterial agents such as clindamycin phosphate, erythromycin or the tetracycline class of antibiotics; antiparasitic agents, in particular metronidazol, crotamiton or pyrethrinoids; antifungal agents, in particular compounds belonging to the class of imidazoles such as econazole, ketoconazole or miconazole or salts thereof, polyene compounds such as amphotericin B, compounds of the family of allylamines, such as terbinafine or alternatively octopirox; steroidal anti-inflammatory agents such as hydrocortisone, anthralins (dioxyanthranol), anthranoids, betamethasone valerate or clobetasol propionate, or non-steroidal anti-inflammatory agents such as ibuprofen and salts thereof, diclofenac and salts thereof, acetylsalicylic acid, acetaminophen or glycyrrhetinic acid; anaesthetic agents such as lidocaine hydrochloride and derivatives thereof; antipruritic agents such as thenaldine, trimeprazine or cyproheptadine; antiviral agents such as acyclovir; keratolytic agents such as alpha- and beta-hydroxycarboxylic or beta-ketocarboxylic acids, their salts, amides or esters and more particularly the hydroxy acids such as glycolic acid, lactic acid, malic acid, salicylic acid, citric acid and, in general, the fruit acids, and 5-n-octanoylsalicylic acid; anti-free radical agents such as alpha-tocopherol or esters thereof, superoxide dismutases, certain metal chelators or ascorbic acid and esters thereof; antiseborrhoeic agents such as progesterone; antidandruff agents such as octopirox or zinc pyrithione; anti-acne agents such as retinoic acid, benzoyl peroxide or adapalene; antimetabolites; agents for combating hair loss such as minoxidil; antiseptics.

Advantageously, the compositions according to the invention comprise from 0.0001% to 20% by weight relative to the total weight of the composition of at least one active agent, preferably from 0.025% to 15% by weight.

Of course, the amount of active agent in the compositions according to the invention will depend on the active agent under consideration. Thus, for a steroidal anti-inflammatory agent, the compositions according to the invention will advantageously comprise less than 1% by weight of active agent, preferably from 0.025% to 0.05% by weight. For the hydroquinones, the compositions according to the invention will preferably comprise from 2% to 5% of active agent. For the antibacterial or antifungal agents such as econazole, the compositions of this invention will preferably comprise from 8% to 10% by weight of active agent.

The fatty phase of the emulsion according to the invention may comprise fatty substances normally used in the intended field of application.

Among these, representative are the silicone fatty substances such as the silicone oils, as well as the non-silicone fatty substances such as the vegetable, mineral, animal or synthetic oils.

Exemplary silicone fatty substances include:

(i) the poly(C_1–C_{20} alkyl)siloxanes and, in particular, those having trimethylsilyl terminal groups, preferably those whose viscosity is less than 0.06 m^2/s, among which are included the linear polydimethylsiloxanes and the alkylmethylpolysiloxanes such as cetyldimethicone (CTFA name),

(ii) the volatile silicone oils, such as:

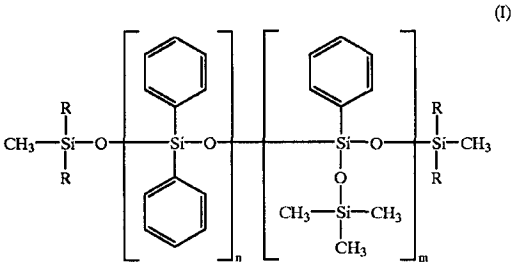
(a) the cyclic volatile silicones having from 3 to 8 silicon atoms and preferably from 4 to 5; these include, for example, cyclotetradimethylsiloxane, cyclopentadimethylsiloxane or cyclohexadimethylsiloxane,

(b) the cyclocopolymers of the dimethylsiloxane/methylalkylsiloxane type, such as SILICONE FZ 3109 marketed by UNION CARBIDE, which is a dimethylsiloxane/methyloctylsiloxane cyclocopolymer,

(c) the linear volatile silicones having from 2 to 9 silicon atoms; these include, for example, hexamethyldisiloxane, hexyl heptamethyltrisiloxane or octyl heptamethyltrisiloxane,

(iii) the phenylated silicone oils, in particular those having the structural formula (I):

(I)



in which R is a C_1–C_{30} alkyl radical, an aryl radical or an aralkyl radical; n is an integer ranging from 0 to 100, and m is an integer ranging from 0 to 100, with the proviso that the sum n+m ranges from 1 to 100.

Among the nonsilicone fatty substances, exemplary are the conventional oils such as paraffin oil, petroleum jelly, almond oil, perhydrosqualene, apricot oil, wheat germ, sweet almond, calophyllum, palm, castor, avocado, jojoba, olive or cereal germ oil; esters of fatty acids or of fatty alcohols, such as octyl dodecyl myristate or C_{12}–C_{15} alkyl benzoates, alcohols; acetylglycerides; octanoates, decanoates or ricinoleates of alcohols or of polyalcohols; triglycerides of fatty acids; glycerides; hydrogenated polyisobutene, hydrogenated oils which are solid at 25° C.; lanolins; fatty esters which are solid at 25° C.

These fatty substances may, in particular, be variously selected by one skilled in this art such as to provide a composition having the desired properties, for example as regards consistency or texture.

Thus, the fatty phase of the emulsion according to the invention may constitute from 5% to 50% by weight relative to the total weight of the composition, and preferably from 15% to 25% by weight.

The aqueous phase of the emulsions according to the invention may comprise water, a floral water such as cornflower water, or a natural mineral or thermal water, for example selected from among Vittel water, water from the Vichy basin, Uriage water, Roche Posay water, Bourboule water, Enghien-les-Bains water, Saint Gervais-les-Bains water, Nèris-les-Bains water, Allevard-les-Bains water, Digne water, Maizières water, Neyrac-les-Bains water, Lons-le-Saunier water, Bonnes water, Rochefort water, Saint

Christau water, Fumades water, Tercis-les-bains water, Avène water or Aix les Bains water.

The aqueous phase advantageously comprises from 10% to 70% by weight relative to the total weight of the composition, preferably from 20% to 40% by weight.

The pH of the compositions according to the invention advantageously ranges from 5 to 7, preferably from 5.5 to 6.5. It will be adjusted to the desired value by adding customary inorganic or organic bases or acids.

Moreover, the compositions according to the invention may comprise from 0% to 3% by weight, preferably from 0% to 2% by weight, relative to the total weight of the composition, of at least one coemulsifier which is advantageously selected from among esters of saturated or unsaturated fatty acids, which are natural or synthetic, in particular oleic acid or (iso)stearic acid, such as the esters of polyglycerin and isostearic acid which are marketed under the trademark LAMEFORM TGI by SIDOBRE-SINNOVA HENKEL, sorbitan isostearate marketed under the trade mark ARLACEL 987 by ICI, sorbitan sesquioleate marketed under the trademark ARLACEL 83 by ICI, the esters of glycol and isostearic acid such as PEG-6 isostearate marketed under the trademark OLEPAL ISOSTEARIQUE by GATTEFOSSE, the esters of sorbitol and oleic acid such as the polysorbates marketed under the trademark TWEEN by ICI, the fatty alcohol ethers, in particular oleyl alcohol, in particular the esters of glycol and oleyl alcohol, such as the oleths marketed under the trademark BRIJ by ICI, oxyethylenated sorbitan monostearate, the fatty alcohols such as stearyl alcohol or cetyl alcohol.

In addition, the compositions according to the invention may comprise at least one gelling and/or thickening agent in preferred concentrations ranging from 0% to 5% by weight relative to the total weight of the composition.

The gelling and/or thickening agent is advantageously selected from among:

(a) the polysaccharide biopolymers such as xanthan gum, carob gum, guar gum, alginates, modified celluloses such as hydroxyethylcellulose, methylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carboxymethylcellulose,

(b) the synthetic polymers such as the polyacrylic acids, for example, glyceryl poly(meth)acrylate polymers such as HISPAGEL or LUBRAGEL marketed by HISPANO QUIMICA or GARDIAN, polyvinylpyrrolidone, polyvinyl alcohol, the crosslinked polymers of acrylamide and ammonium acrylate such as PAS 5161 or BOZEPOL C marketed by HOECHST, the crosslinked polymers of acrylamide and partially or completely neutralized 2-acrylamido-2-methylpropanesulfonic acid such as SEPIGEL 305 marleted by SEPPIC, the crosslinked polymers of acrylamide and methacryloyloxyethyltrimethylammonium chloride such as SALCARE SC 92 marketed by ALLIED COLLOIDS, the crosslinked polymers of acrylic acid and alkyl ethers of sucrose or of pentaerythritol (carbomers) such as CARBOPOL 910 to 934 marketed by GOODRICH.

The subject emulsions may comprise, in addition, any additive or adjuvant customarily employed in the cosmetic or pharmaceutical field, such as antioxidants, colorants, perfumes, essential oils, preservatives, cosmetic active agents, moisturizers, vitamins, essential fatty acids, sphingolipids, selftanning compounds such as DHA, sunscreening agents, fat-soluble polymers, in particular those which contain hydrocarbons, such as polybutene, polyalkylenes, polyacrylates and silicone polymers which are compatible with fatty substances. Of course, one skilled in this art will take care to select this or these possible additional compound(s), and/or their quantity, such that the advantageous properties of the compositions according to the invention are not, or not substantially, altered by the intended addition.

These additives and adjuvants may be present in the subject compositions in an amount of 0% to 10% by weight relative to the total weight of the composition.

In order to further illustrate the present invention and the advantages thereof, the following specific examples are given, it being understood that same are intended only as illustrative and in nowise limitative.

In said examples to follow, all parts and percentages are given by weight.

EXAMPLE 1

Example of a Specific Formulation According to the Invention

COMPOSITION:	% by weight
Purified water	qs 100
Hydroxypropylmethylcellulose	0.10
Propylene glycol	47.50
Active agent	0.05
Liquid paraffin 110–230	20.00
Acrylate/C_{10}–C_{30} alkyl acrylate crosslinked polymer (marketed under the trademark PEMULEN TR-2 by GOODRICH)	0.30
PEG-6 isostearate	2.00
NaOH, 10%	qs *pH 6*

In this formulation, the active agent remained stable for at least 3 months at 40° C.

EXAMPLE 2

Activity of Formulation Comprising Clobetasol Propionate

The formulation of Example 1 according to the invention comprised clobetasol propionate as the active agent.

Vasoconstriction tests according to the modified Stoughton protocol were performed in comparison with the corresponding O/W cream marketed under the trademark TEMOVATE by GLAXO.

The results evidenced an identical bioactivity for the two formulae, which confirmed that, despite the modification of the viscosity of the formulation according to the invention and the use of a different emulsifying system, the pro-penetrating glycol retained its pro-penetrating properties.

While the invention has been described in terms of various preferred embodiments, the skilled artisan will appreciate that various modifications, substitutions, omissions, and changes may be made without departing from the spirit thereof. Accordingly, it is intended that the scope of the present invention be limited solely by the scope of the following claims, including equivalents thereof.

What is claimed is:

1. A stable, topically applicable oil-in-water emulsion which is topically applicable to skin having intermediate viscosity, comprising (a) from 30% to 50% by weight relative to the total weight of said emulsion of at least one glycol, (b) at least one emulsifying agent comprising an

anionic amphiphilic polymer, and (c) at least one biologically active agent, wherein said anionic amphiphilic polymer is present in an amount which in the absence of another emulsifying agent results in an emulsion having an intermediate viscosity, wherein said intermediate viscosity is a viscosity which ranges from 3 to 10 Pa·s (3,000 to 10,000 centipoises), measured with a Brookfield viscometer LVDV II+paddle No. 4, at a speed of 30 revolutions/minutes for thirty seconds, and at a temperature of 25° C.±3° C.

2. The oil-in-water emulsion as defined by claim **1**, comprising up to 5% by weight relative to the total weight of said emulsion of at least one gelling and/or thickening agent.

3. The oil-in-water emulsion as defined by claim **1**, having a pH ranging from 5 to 7.

4. The oil-in-water emulsion as defined by claim **3**, having a pH ranging from 5.5 to 6.5.

5. The oil-in-water emulsion as defined by claim **1**, wherein said at least one polymeric emulsifier is a crosslinked anionic amphiphilic polymer.

6. The oil-in-water emulsion as defined by claim **1**, said anionic amphiphilic polymer comprising the copolymerizate of olefinically unsaturated carboxylic and C_{10}–C_{30} alkyl ester comonomers.

7. The oil-in-water emulsion as defined by claim **5**, said anionic amphiphilic polymer being crosslinked with olefinically unsaturated and non-conjugated polyolefinically unsaturated comonomers.

8. The oil-in-water emulsion as defined by claim **7**, said non-conjugated polyolefinically unsaturated comonomer comprising a polyallyl ether.

9. The oil-in-water emulsion as defined by claim **5**, said crosslinked anionic amphiphilic polymer comprising from 95% to 60% by weight of recurring acrylic structural units, from 4% to 40% by weight of recurring acrylate structural units, and 0.1% to 6% by weight of a crosslinking comonomer, wherein said percentages are relative to the total weight of said emulsion.

10. The oil-in-water emulsion as defined by claim **5**, said crosslinked anionic amphiphilic polymer comprising from 98% to 96% by weight of recurring acrylic structural units, from 1% to 4% by weight of recurring acrylate structural units, and 0.1% to 0.6% by weight of a crosslinking comonomer, wherein said weight percentages are relative to the total weight of said emulsion.

11. The oil-in-water emulsion as defined by claim **1**, comprising up to 1% by weight of said at least one emulsifying agent (b).

12. The oil-in-water emulsion as defined by claim **11**, comprising from 0.2% to 0.4% by weight of said at least one emulsifying agent (b).

13. The oil-in-water emulsion as defined by claim **1**, said at least one glycol (a) comprising a glycol, which promotes penetration of said emulsion into the skin selected from a glycol selected from the group consisting of propylene glycol, dipropylene glycol, propylene glycol dipelargonate, lauroglycol and ethoxydiglycol.

14. The oil-in-water emulsion as defined by claim **13**, comprising from 40% to 50% by weight relative to the total weight of said emulsion of said at least one glycol (a).

15. The oil-in-water emulsion as defined by claim **2**, said at least one biologically active agent is selected from the group consisting of (c) an agent which modulates at least one of skin differentiation, proliferation and pigmentation; an antibacterial agent, an antiparasitic agent, an antifungal agent, a steroidal anti-inflammatory agent, a non-steroidal anti-inflammatory agent, an anaesthetic agent, an antipruritic agent, an antiviral agent, a keratolytic agent, an anti-free radical agent, an antiseborrhoeic agent, an antidandruff agent, an anti-acne agent, an antimetabolite, an agent for combating hair loss, an antiseptic and combinations thereof.

16. The oil-in-water emulsion as defined by claim **15**, comprising from 0.0001% to 20% by weight relative to the total weight of said emulsion of said at least one biologically active agent (c).

17. The oil-in-water emulsion as defined by claim **1**, comprising from 5% to 50% by weight relative to the total weight of said emulsion of an oily phase.

18. The oil-in-water emulsion as defined by claim **17**, comprising from 10% to 70% by weight of an aqueous phase relative to the total weight of said emulsion.

19. The composition of claim **1**, wherein said anionic amphiphilic polymer comprises recurring acrylic structural units and acrylate structural units.

20. The composition of claim **2**, wherein said anionic amphiphilic polymer is cross-linked.

* * * * *

EXHIBIT "B"

actavis
creating value in pharmaceuticals

RECEIVED
MAY 25 2006
PAUL CLARK

May 22, 2006

VIA UPS OVERNITE-#J170 911 072 8
Humberto C. Antunes, President & CEO
Galderma S.A.
World Trade Center
Avenue de Gratta-Paille 1
Cose Postale 453
1000 Lausanne 30 Grey
Switzerland

VIA REGISTERED MAIL
RETURN RECEIPT REQUESTED
Paul Clark, Vice President Regulatory Affairs
Galderma Labs LP
14501 North Freeway
Fort Worth, TX 76177

Re: Clobetasol Propionate Lotion, 0.05%
Paragraph IV Certification for U.S. Patent No. 6,106,848

Dear Sirs:

Actavis Mid Atlantic LLC. ("Actavis"), formerly known as Alpharma USPD, is providing the following information pursuant to § 505(j)(2)(B)(ii) of the Federal Food, Drug, and Cosmetic Act ("the Act"):

1. In order to obtain approval to engage in the commercial manufacture, use or sale of Clobetasol Propionate Lotion 0.05% (the "PROPOSED PRODUCT"), Actavis submitted to the Food and Drug Administration ("FDA") an Abbreviated New Drug Application ("ANDA") under § 505(j) of the Act that contains the required bioavailability or bioequivalence data or information. The FDA has documented the receipt of this application and has notified Actavis accordingly.

2. The ANDA number is 78-223.

3. The established name for the proposed drug product is Clobetasol Propionate Lotion, 0.05%. Galderma markets Clobetasol Propionate Lotion, 0.05% under the brand name Clobex®.

4. The active ingredient, strength, and dosage form of the proposed drug product is Clobetasol Proprionate, 0.05%, lotion.

5. The ANDA indicates that Actavis intends to market the product before the expiration date of U.S Patent No.. Actavis believes this patent was identified to the FDA for listing in the Orange Book.

The ANDA indicates that the claims of U.S. Patent No. 6,106,848 are invalid and/or will not be infringed by the commercial manufacture, use or sale of the proposed drug product. Below is a detailed statement of the factual and legal bases for Actavis's conclusions. This information is supplied for the sole purpose of complying with the above-referenced statutes. Accordingly, Actavis does not waive any attorney-client privilege or work product immunity concerning the subject matter of this communication.

In addition, for the sole purpose of allowing you to determine whether an action referred to in 21 U.S.C. § 355(j)(5)(B)(iii) should be brought, Actavis hereby offers to provide confidential access to ANDA No. 78-223, subject to the restrictions set forth in the attached Offer of Confidential Access and Confidentiality Agreement (the "Agreement"). If you should desire such confidential access, please execute the Agreement and contact me to make the appropriate arrangements.

DETAILED ANALYSIS

Actavis' manufacture, use, importation, offer for sale, and/or sale of the PROPOSED PRODUCT would not infringe any one of the claims of the '848 patent literally or under the doctrine of equivalents.

The '848 patent generally discloses oil-in-water emulsions having a viscosity of 3 to 10 Pascal-seconds, comprising (a) from 30% to 50% by weight of at least one pro-penetrating glycol, (b) at least one emulsifying agent, advantageously an anionic amphiphilic polymer, and (c) at least one biologically active agent. Claim 1, the only independent claim, requires "an emulsifying agent comprising an anionic amphiphilic polymer". The PROPOSED PRODUCT would not infringe claim 1 because it will not contain an anionic amphiphilic polymer. Because this

claim is the broadest claim in the '848 patent, the PROPOSED PRODUCT also would not infringe any of the dependent claims, claims 2-20.

Furthermore the PROPOSED PRODUCT would not infringe any of the claims of the '848 patent under the doctrine of equivalents. Specifically, prosecution history estoppel would prevent use of the doctrine of equivalents to expand the scope of the limitation requiring use of "an emulsifying agent comprising an anionic amphiphilic polymer" to cover any of the components of the PROPOSED PRODUCT. Prosecution history estoppel applies in this case because an amendment filed during prosecution of the '848 patent narrowed the literal scope of the claim; the reason for the amendment was a substantial one relating to the patentability of the invention; and we see no basis for the patentee to rebut the presumption that all territory between the original claim limitation ("at least one emulsifying agent") and the amended claim limitation ("at least one emulsifying agent comprising an anionic amphiphilic polymer") was surrendered.

II. BACKGROUND

A. The PROPOSED PRODUCT

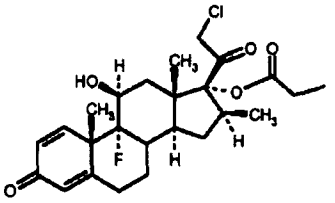
The PROPOSED PRODUCT is a 0.5 weight percent clobetasol propionate lotion and consists only of the components shown in Table 1

Table 1.

Component (Trade name)	Function
Clobetasol propionate, USP	Active pharmaceutical ingredient
Hydroxypropyl methylcellulose, USP (Benecel® MP824 PH, type 2208)	Thickener (imparts viscosity to lotion composition)
Polyoxyethylene 6 isostearate (Polyoxyl-6 Isostearate, Olepal Isostearique)	Emulsifier
Mineral oil, USP	Oil component of emulsion
Propylene glycol, USP	Solubilize active pharmaceutical ingredient
Sodium hydroxide, NF	pH adjustment
Poly(acrylic acid) (Carbomer® 940)	Thickener (imparts viscosity to lotion composition)
Polyoxyethylene 20 sorbitan monooleate (Polysorbate 80)	Emulsifier

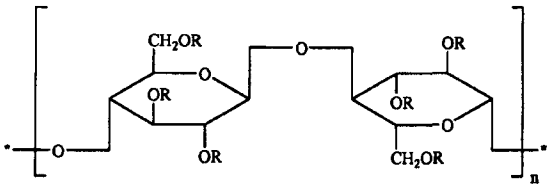
Purified water, USP	Aqueous component of emulsion

Clobetasol propionate (Chemical Abstracts Registry No. 25122-46-7), the active pharmaceutical ingredient, is a corticosteroid used for the treatment of skin conditions. Its chemical structure is shown below.



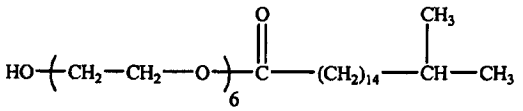
Clobetasol propionate is not a polymer.

Hydroxypropyl methylcellulose, also known as Hypromellose, is a partly O-methylated and O-(2-hydroxypropylated) cellulose. Handbook of Pharmaceutical Excipients, entry for Hypromellose, pp. 297-300. It has the chemical structure shown below,



where R is -H, $-CH_3$, or $-CH_2CH(OH)CH_3$; and n is a repeat unit sufficient to give a molecular weight of about 10,000 to about 1,500,000. Hypromellose is a nonionic polymer. *Id.* at p. 299, column 1, item **12** "Incompatibilities".

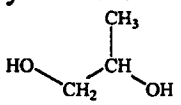
Polyoxyethylene 6 isostearate is a fatty acid monoester of a polyoxyethylene having six oxyethylene repeat units. The generic class of polyoxyethylene stearates are described in the Handbook of Pharmaceutical Excipients. Handbook of Pharmaceutical Excipients, entry for Polyoxyethylene Stearates, pp. 484-487. See also, the structure of polyethylene glycol isostearate, Chemical Abstracts Registry record for polyethylene glycol isostearate, Registry No. 56002-14-3. Based on these sources, the chemical structure of polyoxyethylene 6 isostearate is given below.



Polyoxyethylene stearates are nonionic surfactants. Handbook of Pharmaceutical Excipients, entry for Polyoxyethylene stearates, p. 484, column 1, item 2 "Synonyms".

Mineral oil is a mixture of refined liquid saturated aliphatic (C_{14}-C_{18}) and cyclic hydrocarbons obtained from petroleum. Handbook of Pharmaceutical Excipients, entry for Mineral Oil, pp. 395-397. Mineral oil is not a polymer. Mineral oil is also not amphiphilic, because it does not have any hydrophilic groups.

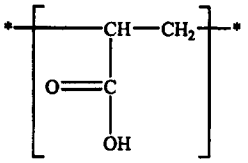
Propylene glycol, also known as 2-hydroxypropanol, is a C_3 dialcohol. Handbook of Pharmaceutical Excipients, entry for Propylene glycol, pp. 521-523. The chemical structure of propylene glycol is shown below.



Propylene glycol is not a polymer.

Sodium hydroxide is a strong base used for pH adjustment. Handbook of Pharmaceutical Excipients, entry for Sodium Hydroxide, pp. 566-567. Sodium hydroxide is not a polymer.

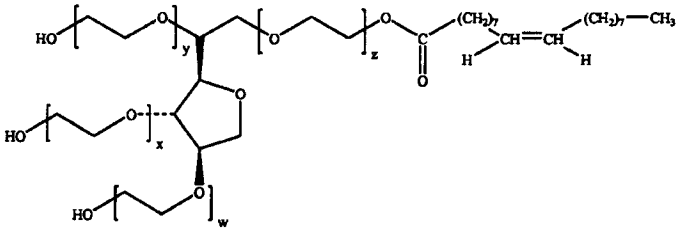
Poly(acrylic acid), also known as Carbomer, is an acrylic acid polymer. Handbook of Pharmaceutical Excipients, entry for Carbomer, pp. 89-92. The chemical structure of the repeating unit of poly(acrylic acid) is given below.



Poly(acrylic acid) is used in the PROPOSED PRODUCT as a viscosity increasing agent. Poly(acrylic acid) is not amphiphilic because it does not contain a hydrophobic group.

Polyoxyethylene 20 sorbitan monooleate is a fatty acid monoester of a polyoxyethylene sorbitan. It has twenty oxyethylene repeat units. Handbook of Pharmaceutical Excipients, entry for Polyoxyethylene Sorbitan Fatty Acid Esters, pp. 479-483. The Chemical Abstracts Registry record for polyoxyethylene 20 sorbitan monooleate does not include a chemical structure. However, the chemical structure can be deduced from the known general structure of

polyoxyethylene sorbitan monoesters, *id.*, and the known structure of oleic acid. Chemical Abstract Registry File record for oleic acid, Registry No. 112-80-1. The chemical structure is shown below,



where w + x + y + z = 20. Polysorbates containing twenty oxyethylene units, including polyoxyethylene 20 sorbitan monooleate, are nonionic surfactants. Handbook of Pharmaceutical Excipients, entry for Polyoxyethylene Sorbitan Fatty Acid Esters, p. 480, column 1, item 6 "Functional Category".

B. The '848 Patent

The '848 patent is directed to topically applicable oil-in-water emulsions containing a biologically active agent. '848 Patent, Abstract. The oil-in-water emulsions have a viscosity of 3 to 10 Pascal-seconds, and they contain 30 to 50 weight percent of at least one pro-penetrating glycol, at least one emulsifying agent that is preferably an anionic amphiphilic polymer, and at least one biologically active agent. *Id.*

1. The Claims of the '848 Patent

The '848 patent includes twenty claims consisting of one independent claim (claim 1) and nineteen dependent claims. Claim 1 is reproduced below (formatting added).

> 1. A stable, topically applicable oil-in-water emulsion which is topically applicable to skin having intermediate viscosity, comprising
>
> (a) from 30% to 50% by weight relative to the total weight of said emulsion of at least one glycol,
>
> (b) at least one emulsifying agent comprising an anionic amphiphilic polymer, and
>
> (c) at least one biologically active agent,
>
> wherein said anionic amphiphilic polymer is present in an amount which in the absence of another emulsifying agent results in an emulsion having an intermediate viscosity,

> wherein said intermediate viscosity is a viscosity which ranges from 3 to 10 Pa·s (3,000 to 10,000 centipoises), measured with a Brookfield viscometer LVDV II+paddle No. 4, at a speed of 30 revolutions/minutes for thirty seconds, and at a temperature of 25° C.±3° C.

Claim 1 thus requires the presence of "an anionic amphiphilic polymer" and further sets a functional lower limit on the amount of anionic amphiphilic polymer, by specifying that it is present "in an amount which in the absence of another emulsifying agent results in an emulsion having an intermediate viscosity . . . which ranges from 3 to 10 Pa·s" measured on a particular instrument at 25° C.±3° C.

Claim 2 recites the presence of "at least one gelling and/or thickening agent" which is impliedly distinct from the anionic amphiphilic polymer.

> 2. The oil-in-water emulsion as defined by claim 1, comprising up to 5% by weight relative to the total weight of said emulsion of at least one gelling and/or thickening agent.

Many of the dependent claims further specify the type and amount of the anionic amphiphilic polymer. Claim 20, depending from claim 2, specifies that the anionic amphiphilic polymer is crosslinked.

> 20. The composition of claim 2, wherein said anionic amphiphilic polymer is cross-linked.

Claim 3, depending from claim 1, specifies an emulsion pH range of 5 to 7.

> 3. The oil-in-water emulsion as defined by claim 1, having a pH ranging from 5 to 7.

Claim 5, depending from claim 1, specifies that the anionic amphiphilic polymer is crosslinked.

> 5. The oil-in-water emulsion as defined by claim 1, wherein said at least one polymeric emulsifier is a crosslinked anionic amphiphilic polymer.

Claim 7, depending from claim 5, recites particular crosslinking monomers used to prepare the crosslinked anionic amphiphilic polymer.

> 7. The oil-in-water emulsion as defined by claim 5, said anionic amphiphilic polymer being crosslinked with olefinically unsaturated and non-conjugated polyolefinically unsaturated comonomers.

Claims 9 and 10, each depending from claim 5, specify particular comonomer types and amounts used to prepare the anionic amphiphilic polymer.

> 9. The oil-in-water emulsion as defined by claim 5, said crosslinked anionic amphiphilic polymer comprising from 95% to 60% by weight of recurring acrylic structural units, from 4% to 40% by weight of recurring acrylate structural units, and 0.1% to 6% by weight of a crosslinking comonomer, wherein said percentages are relative to the total weight of said emulsion.

> 10. The oil-in-water emulsion as defined by claim 5, said crosslinked anionic amphiphilic polymer comprising from 98% to 96% by weight of recurring acrylic structural units, from 1% to 4% by weight of recurring acrylate structural units, and 0.1% to 0.6% by weight of a crosslinking comonomer, wherein said weight percentages are relative to the total weight of said emulsion.

Claim 6, depending from claim 1, describes the anionic amphiphilic polymer as the copolymerization product of two particular types of monomers.

> 6. The oil-in-water emulsion as defined by claim 1, said anionic amphiphilic polymer comprising the copolymerizate of olefinically unsaturated carboxylic and C_{10}-C_{30} alkyl ester comonomers.

Claim 11, depending from claim 1, sets an upper limit on the amount of the anionic emulsifying agent.

> 11. The oil-in-water emulsion as defined by claim 1, comprising up to 1% by weight of said at least one emulsifying agent (b).

Claim 19, depending from claim 1, specifies that the anionic amphiphilic polymer includes at least two particular types of repeat units.

19. The composition of claim 1, wherein said anionic amphiphilic polymer comprises recurring acrylic structural units and acrylate structural units.

2. The Specification of the '848 Patent

The BACKGROUND OF THE INVENTION section of the '848 patent describes existing topical compositions with high glycol content and divides them into low-viscosity "hair lotions" and high-viscosity oil-in-water creams or "O/W creams".

> Currently marketed are numerous topical compositions comprising an active agent and a high content of glycol, the latter promoting the penetration of the biologically active agent into the skin. Given the high content of pro-penetrating glycol, these compositions are formulated as emulsions having a high content of fatty phase which are also commonly designated "lipocreams," as anhydrous compositions which are deemed "ointments," as fluid compositions having a high content of volatile solvents, such as ethanol or isopropanol, which are destined for application to the scalp, i.e., "hair lotions," or, alternatively, as viscous O/W emulsions which are also designated "O/W creams."
>
> O/W creams comprising a corticoid and including a high percentage of propylene glycol (47.5%), which are marketed under the trademark TEMOVATE® by GLAXO, are known to this art. Indeed, the stabilization of a formulation comprising such a percentage of glycol necessitates incorporating, in the emulsion, emulsifying and stabilizing agents of the glyceryl stearate or PEG 100 stearate type or, alternatively, stabilizing agents or consistency factors of the white wax or ketostearyl alcohol type which form a viscous cream, namely, whose viscosity is greater than 10 Pa·s (10,000 centipoises, measured with a Brookfield apparatus model LVDV II+paddle No. 4, at a speed of 30 revolutions/min for 30 seconds and at a temperature of 25° C.± 3° C.).

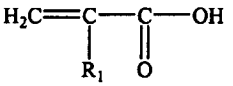
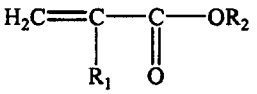
'848 Patent, col. 1, lines 30-42. Note that prior art high-viscosity compositions containing "emulsifying and stabilizing agents of the glyceryl stearate or PEG 100 stearate type" are specifically mentioned. '848 Patent, col. 1, lines 35-36.

The invention of the '848 patent is distinguished as providing a viscosity intermediate between that of low-viscosity "hair lotions" and high-viscosity "O/W creams". '848 Patent, col. 1, lines 43-50 and col. 1, lines 64-66.

The composition is generally described as containing a "polymeric emulsifier", more particularly an "anionic amphiphilic polymer", but neither these terms nor their component parts (such as "anionic" and "amphiphilic") are specifically defined. Rather, a specific type of "anionic amphiphilic polymer" is described.

> Advantageously, a stable emulsion is provided according to the invention by selecting, as an appropriate emulsifying system, at least one polymeric emulsifier. The polymeric emulsifiers are in particular described by CLYMANS & BRAND in "Cosmetics and Toiletries" (manufacture worldwide, 1995, 119-125).
>
> These are, in particular, anionic amphiphilic polymers, more especially those comprising at least one hydrophilic recurring structural unit of the unsaturated olefin carboxylic acid type, and at least one hydrophobic recurring structural unit of the C_{10}-C_{30} alkyl ester type.

'848 Patent, col. 2, lines 4-14. Comonomers used to form the anionic amphiphilic polymers are described as follows.

> According to the invention, acrylic structural units are those of the formula:
>
> 
>
> in which R_1 is H, CH_3 or C_2H_5, namely, acrylic acid, methacrylic acid or ethacrylic acid structural units.
>
> Alkyl acrylate structural units are those of the formula:
>
> 
>
> in which R_1 is H, CH_3 or C_2H_5, namely, acrylate, methacrylate or ethacrylate units, and R_2 is a C_{10}-C_{30}, preferably C_{12}-C_{22}, alkyl radical.
>
> Exemplary acrylates according to the invention include lauryl acrylate, stearyl acrylate, decyl acrylate, isodecyl acrylate, dodecyl acrylate and the corresponding methacrylates, lauryl

> methacrylate, stearyl methacrylate, decyl methacrylate, isodecyl methacrylate and dodecyl methacrylate.

'848 Patent, col. 2, lines 15-39. It is clear from the context of this section of the '848 patent that the "acrylic structural units" are a type of "hydrophilic recurring structural unit of the unsaturated olefin carboxylic acid type", and the "alkyl acrylate structural units" are a type of "hydrophobic recurring structural unit of the C_{10}-C_{30} alkyl ester type". '848 Patent, col. 2, lines 10-39.

Preferred anionic amphiphilic polymers containing crosslinks are described as follows.

> Preferably, the above anionic amphiphilic polymers are crosslinked using a crosslinking polymerizable comonomer containing a CH_2=C< group with at least one other polymerizable group whose sites of unsaturation are not conjugated relative to each other.
>
> Exemplary such crosslinking polymerizable comonomers preferably include polyallyl ethers such as, in particular, polyallylsucrose and polyallylpentaerythritol.
>
> Crosslinked polymers of this type are well known to this art; they are, in particular, described in U.S. Pat. Nos. 3,915,921 and 4,509,949.

'848 Patent, col. 2, lines 40-50. Preferred and more preferred monomer compositions of crosslinked anionic amphiphilic polymers are also described, as are commercial sources of crosslinked polymers.

> According to the invention, anionic amphiphilic polymers are preferred which comprise 95% to 60% by weight of acrylic recurring structural units, 4% to 40% by weight of acrylate recurring structural units and 0.1% to 6% by weight of crosslinking monomer, or (ii) which comprise 98% to 96% by weight of acrylic recurring structural units, 1% to 4% by weight of acrylate recurring structural units and 0.1% to 0.6% by weight of crosslinking monomer.
>
> Among said crosslinked polymers indicated above, those marketed by GOODRICH under the trademarks PEMULEN TR1, PEMULEN TR2, CARBOPOL 1342 and CARBOPOL 1382 are most particularly preferred according to the present invention.

'848 Patent, col. 2, lines 51-58.

The amount of the polymeric emulsifier is functionally limited by the requirement that the composition have a viscosity of 3 to 10 Pascal-seconds at 25±3°C. '848 Patent, col. 1, lines 64-66. The written description does not express absolute upper and lower limits of emulsifier concentration, but preferences are given for emulsifier concentrations of "up to 1[%] by weight" and "from 0.2% to 0.4% by weight", based on the total weight of the composition. '848 Patent, col. 2, lines 64-67.

The pH of the composition "advantageously ranges from 5 to 7, preferably from 5.5 to 6.5". '848 Patent, col. 5, lines 6-8.

In addition to the emulsifier, which is an anionic amphiphilic polymer, the composition may contain up to 3% by weight of one or more "coemulsifiers".

> Moreover, the compositions according to the invention may comprise from 0% to 3% by weight, preferably from 0% to 2% by weight, relative to the total weight of the composition, of at least one coemulsifier which is advantageously selected from among esters of saturated or unsaturated fatty acids, which are natural or synthetic, in particular oleic acid or (iso)stearic acid, such as the esters of polyglycerin and isostearic acid which are marketed under the trademark LAMEFORM TGI by SIDOBRE-SINNOVA HENKEL, sorbitan isostearate marketed under the trade mark ARLACEL 987 by ICI, sorbitan sesquioleate marketed under the trademark ARLACEL 83 by ICI, the esters of glycol and isostearic acid such as PEG-6 isostearate marketed under the trademark OLEPAL ISOSTEARIQUE by GATTEFOSSE, the esters of sorbitol and oleic acid such as the polysorbates marketed under the trademark TWEEN by ICI, the fatty alcohol ethers, in particular oleyl alcohol, in particular the esters of glycol and oleyl alcohol, such as the oleths marketed under the trademark BRIJ by ICI, oxyethylenated sorbitan monostearate, the fatty alcohols such as stearyl alcohol or cetyl alcohol.

'848 Patent, col. 5, lines 10-30. Note, in particular, that the coemulsifiers include "PEG-6 isostearate marketed under the trademark OLEPAL ISOSTEARIQUE by

GATTEFOSSE" and "the esters of sorbitol and oleic acid such as the polysorbates marketed under the trademark TWEEN by ICI".

The composition may also include 0-5% by weight of a "gelling and/or thickening agent". '848 Patent, col. 5, lines 31-34. Among the gelling and/or thickening agents mentioned are "hydroxypropylmethylcellulose" and "polyacrylic acids". '848 Patent, col. 5, lines 40-42.

3. The Prosecution History of the '848 Patent

The '848 patent was issued from U.S. Patent Application Serial No. 08/935,054 filed on Monday, September 22, 1997 and claiming priority to French Patent Application Serial No. 96 11510, filed September 20, 1996. The '054 application included twenty-two claims, with claim 1 being the only independent claim. Claim 1 as filed is reproduced below.

> 1. A stable, topically applicable oil-in-water emulsion having intermediate viscosity, comprising (a) from 30% to 50% by weight of at least one glycol, (b) at least one emulsifying agent, and (c) at least one biologically active agent.

The preamble of claim 1 as filed refers to the emulsion "having intermediate viscosity", but that viscosity is not defined within the claim. Note also that there are no compositional or amount limitations associated with the "emulsifying agent".

Claim 2 as filed defined the viscosity value and measurement conditions.

> 2. The oil-in-water emulsion as defined by Claim 1, having a viscosity ranging from 3 to 10 Pa·s (3,000 to 10,000 centipoises), measured with a Brookfield viscosimeter model LVDV II + paddle No. 4, at a speed of 30 revolutions/min for 30 seconds and at a temperature of 25° C.± 3° C.

Claim 3 limited claim 1's "at least one emulsifying agent" to "at least one polymeric emulsifier", and claim 4 limited claim 3's "at least one polymeric emulsifier" to "an anionic amphiphilic polymer".

> 3. The oil-in-water emulsion as defined by Claim 2, said at least one emulsifying agent (b) comprising at least one polymeric emulsifier.
>
> 4. The oil-in-water emulsion as defined by Claim 3, said at least one polymeric emulsifier comprising an anionic amphiphilic polymer.

After a notice of missing parts was issued by the U.S. Patent and Trademark Office ("PTO") and responded to by applicants, the PTO issued a first office action on the merits on May 21, 1998. Claims 1 to 22 (all claims) were rejected under 35 U.S.C. § 112, second paragraph as indefinite because of the following ambiguities.

> It is not clear, what "topically" applies to (plants?) And should be modified to provide clear indication of intended targets. Same is true of "biologically active"-this could mean water, and should be identified in accord with the invention. It is unclear what is meant by "Propenetrating" (claim 13). Claim 15 is unclear: whether the recited agents are the bioactive, or in addition to it if Markush language, or should be and (last line). Re writing of claim to provide clarity is required. It is unclear what the % are based on. Claim 17 has no antecedent for "fatty phase".

5/21/98 Office Action, page 2, last paragraph.

Claims 1-22 were also rejected under 35 U.S.C. § 102(b) as anticipated by or, alternatively, under 35 U.S.C. § 103(a) as obvious over, International Patent Application No. WO 94/17830 of Robert et al. 5/21/98 Office Action, page 3, second paragraph. In making this rejection, the examiner argued that "[e]mulsifier[s] of the instant invention are shown at page 11, first paragraph . . . and also are shown at page 9, as the instant carbopols." 5/21/98 Office Action, page 3, last paragraph.

In an amendment filed September 21, 1998, applicants amended claim 1 to specify that the emulsion "is topically applicable to skin" and that the weight percent of glycol is "relative to the total weight" of emulsion. 9/21/98 Amendment, page 2. Applicants traversed the anticipation rejection over WO 94/17830. 9/21/98 Amendment, page 8, last paragraph. Applicants' primary argument was as follows.

> [The] reference completely fails to teach or suggest a composition as claimed, which comprises at least 30 to 50% by weight of at least one glycol, and which comprises an intermediate viscosity, i.e., a viscosity ranging from 3 to 10 Pa·s when measured with a Brookfield viscosimeter under the conditions recited in Claim 2.

9/21/98 Amendment, page 11, first full paragraph. In response to the examiner's assertion that the carbopols of the reference were the same as the emulsifiers of the instant invention, applicants argued that Carbopol 1382 and Carbopol 1342 were used in the reference "as gelling agents, not as principal emulsifying agents". 9/21/98 Amendment, page 14, first full paragraph.

The PTO responded to applicants' 9/21/98 amendment with a non-final office action mailed 12/15/98. The examiner maintained his rejection of all claims as anticipated by or obvious over WO 94/17380, stating, "all the components as claimed are present and known in the prior art, and when considered in terms of the emulsion, the glycol is of the instant concentration." 12/15/98, paragraph bridging pages 2 and 3.

Applicants then filed a second amendment dated March 15, 1999. Claim 4 was canceled, and claim 1 was amended to incorporate the limitation of claim 4 using "consisting essentially of" terminology, thereby specifying that the composition comprises "at least one emulsifying agent consisting essentially of an anionic amphiphilic polymer".

> 1. (Twice Amended) A stable, topically applicable oil-in-water emulsion which is topically applicable to skin having intermediate viscosity, comprising (a) from 30% to 50% by weight relative to the total weight of said emulsion of at least one glycol, (b) at least one emulsifying agent consisting essentially of an anionic amphiphilic polymer, and (c) at least one biologically active agent.

3/15/99 Amendment, pages 1-2. Applicants argued that WO 94/17830 "fails to teach or suggest a composition as claimed, containing an emulsifying agent which consist *[sic]* essentially of an anionic amphiphilic polymer." 3/15/99 Amendment, page 5, last paragraph. Applicants expressly distinguished the reference's use of Carbopol 1382 or 1342, characterizing these materials "as gelling agents, not as principal emulsifying agents." 3/15/99 Amendment, page 10, second paragraph.

In response to applicants' 3/15/99 amendment, the PTO issued a final office action on June 7, 1999. The examiner made a new indefiniteness rejection of all pending claims (claims 1-3 and 5-22) under 35 U.S.C. § 112, second paragraph because "[i]t is unclear what essentiality [*sic*] is being claimed, functionally" and "[i]t is unclear what is meant by skin of intermediate viscosity" in claim 1. 6/7/99 Office Action, page 2, third and fourth paragraphs. The examiner also maintained his rejection of all claims as anticipated by or obvious over WO 94/17830 for reasons previously of record. 6/7/99 Office Action, pages 2-3.

In response to the 6/7/99 final office action, applicants filed a notice of appeal (not included here) and an amendment after final, both on 9/7/99. Claims 2, 3, and 19 were canceled, and claim 1 was again amended, this time to define within the body of the claim "intermediate viscosity" and the conditions for its measurement.

> 1. (Three times Amended) A stable, topically applicable oil-in-water emulsion which is topically applicable to skin having intermediate viscosity, comprising (a) from 30% to 50% by weight relative to the total weight of said emulsion of at least one glycol, (b) at least one emulsifying agent consisting essentially of an anionic amphiphilic polymer, and (c) at least one biologically active agent, wherein said intermediate viscosity is a viscosity which ranges from 3 to 10 Pa.s (3,000 to 10,000 centipoises), measured with a Brookfield viscometer LVDV II + paddle No. 4, at a speed of 30 revolutions/minutes for thirty seconds, and at a temperature of 25°C ±3°C.

9/7/99 Amendment, paragraph bridging pages 1 and 2. Applicants repeated their argument from the 3/15/99 amendment that the WO 94/17830 "fails to teach or suggest an emulsifying agent which consists essentially of an anionic amphiphilic polymer." 9/7/99 Amendment, page 6, last paragraph. As part of their argument, they again distinguished the emulsifying agents of claim 1 from the Carbopol materials of the reference: "Carbopol 1382 or 1342 are present as gelling agents, not as principal emulsifying agents." 9/7/99 Amendment, page 11, first full paragraph.

The PTO responded to applicants' 9/7/99 amendment with an Advisory Action dated September 16, 1999. The advisory action refused entry of the proposed

amendments as not placing the application in better form for appeal. 9/16/99 Advisory Action, page 1.

The 9/16/99 Advisory Action was followed by an examiner interview by applicants' attorney Robin L. Teskin, on December 21, 1999. The interview is documented in an Examiner Interview Summary Record. The Examiner's handwritten comments are difficult to read, but they appear to say that "claims permitting more than 1 emulsifier 'consisting of' still would permit >1 emulsifier. Claims limited to 1 or more anionic amphiphilic polymers, however would be reconsidered in view of art, & amend. entered."

Applicants then filed a continuing prosecution application on January 6, 2000 (not included here), and a preliminary amendment on January 19, 2000. The preliminary amendment again amended claim 1, this time replacing "consisting essentially of" with "comprising" and adding language to state that the amount of the anionic amphiphilic polymer produces an emulsion viscosity of 3-10 Pascal-seconds in the absence of other emulsifying agents.

> 1. (Four times Amended) A stable, topically applicable oil-in-water emulsion which is topically applicable to skin having intermediate viscosity, comprising (a) from 30% to 50% by weight relative to the total weight of said emulsion of at least one emulsifying agent [consisting essentially of] comprising an anionic amphiphilic polymer, and (c) at least one biologically active agent, wherein said anionic amphiphilic polymer is present in an amount which in the absence of another emulsifying agent results in an emulsion having an intermediate viscosity, wherein said intermediate viscosity is a viscosity which ranges from 3 to 10 Pa.s (3,000 to 10,000 centipoises), measured with a Brookfield viscometer LVDV II + paddle No. 4, at a speed of 30 revolutions/minutes for thirty seconds, and at a temperature of 25°C ±3°C.

1/19/00 Preliminary Amendment, paragraph bridging pages 1 and 2. The preliminary amendment also introduced two new claims, 23, and 24, directed to the structure of the anionic amphiphilic polymer.

> 23. The composition of Claim 1, wherein said anionic amphiphilic polymer comprises recurring acrylic structural units and acrylate structural units.

24. The composition of Claim 23, wherein said anionic amphiphilic polymer is cross-linked.

1/19/00 Preliminary Amendment, page 2, first through third full paragraphs. Applicants commented that "the previous 'consisting essentially of' phraseology has been deleted, as this language was asserted by the Examiner to be ambiguous." 1/19/00 Amendment, page 2, first paragraph.

A notice of allowability followed on March 29, 2000. It gave no reasons for allowance except to state that the notice was responsive to the amendment and remarks filed 1/19/00. 3/29/00 Notice of Allowability.

III. THE PROPOSED PRODUCT DOES NOT INFRINGE THE '848 PATENT'S CLAIMS

Courts analyze infringement in two steps. First, the court determines the meaning and scope of the patent claims asserted to be infringed as a matter of law. Next, the court compares the properly construed claims to the device or method accused of infringing. *Markman v. Westview Instruments Inc.*, 52 F.3d 967, 34 U.S.P.Q.2d 1321 (Fed. Cir. 1995) *(en banc), aff'd*, 116 S.Ct. 1384, 38 U.S.P.Q.2d 1461 (1996).

A. Claim Construction

Claims are always in the form of a single sentence, usually having a preamble and one or more "elements" or "limitations". The limitations of the claims provide the measure for patentability, as well as infringement. To analyze either the validity or infringement of a patent, therefore, the patent claims must first be construed to determine their proper scope and content. *See, e.g., Minnesota Mining and Manufacturing Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1565 (Fed. Cir. 1992). A patent construction, including terms of art within its claim, is exclusively within the province of a judge. *Markman v. Westview Instruments, Inc.*, 116 S.Ct. 1384, 1387, 38 U.S.P.Q.2d 1461, 1463 (1996), *affirming* 52 F.3d 967, 971, 34 U.S.P.Q.2d 1321, 1322 (Fed. Cir. 1995) (*en banc*).

1. Relevant Law of Claim Construction

Words of a claim are generally given their ordinary and customary meaning. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1326, 75 U.S.P.Q.2d 1321, 1326 (Fed. Cir. 2005) (*en banc*), *citing Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582, 39 U.S.P.Q. 1573, 1576 (Fed. Cir. 1996). The ordinary and customary meaning of a claim term is the meaning that the term would have "to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips* at 1313. This meaning was stated by the *Phillips* court to "provide an objective baseline from which to begin claim interpretation." *Id.* Even so, this person of ordinary skill in the art is deemed to have read the claim term not only in the context of the particular claim in which the disputed term appears but also in the context of the entire patent, including the specification and prosecution history of the patent. *Id.* at 1313-1314. Proper construction of a patent claim thus requires consideration of all the sources of meaning of the claim in the PTO record, namely the claim language itself, the written description, and the prosecution history, including the prior art cited during the examination of the patent. *Markman*, 52 F.3d at 979; *Amhil Enterprises Ltd. v. Wawa, Inc.*, 81 F.3d 1554, 1559-62 (Fed. Cir. 1996).

Where the ordinary meaning of a claim term is clear even to the layperson, claim construction "involves little more than the application of the widely accepted meaning of commonly understood words . . . in such circumstances, general purpose dictionaries may be helpful." *Phillips* at 1314. Where terms have a particular meaning to those of skill in the art, a court may look to "extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* (internal quotes omitted). Nonetheless, "the specification 'is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.'" *Id.* at 1315, *citing Vitronics,* 90 F.3d at 1582. "In light of the statutory directive that the inventor provide a 'full' and 'exact' description of the claimed invention, the specification necessarily informs the proper construction of the claims." *Phillips* at 1316.

The *Phillips* court also held that the specification is more useful than the prosecution history for construction purposes because the "prosecution history often lacks the clarity of the specification." *Id.* at 1317. Both of these carry more weight than extrinsic evidence. For example, technical dictionaries can be properly consulted to clarify the accepted meaning of a term in the field of the invention, and expert testimony can be useful to provide background or understand how an invention works, but all extrinsic evidence is "less reliable" than the intrinsic record. *Id.* at 1318. The court summarized, stating:

> [E]xtrinsic evidence may be useful to the court, but it is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence. Nonetheless, because extrinsic evidence can help educate the court regarding the field of the invention and can help the court determine what a person of ordinary skill in the art would understand claim terms to mean, it is permissible for the district court in its sound discretion to admit and use such evidence. In exercising that discretion, and in weighing all the evidence bearing on claim construction, the court should keep in mind the flaws inherent in each type of evidence and assess that evidence accordingly.

Id. at 1319.

A claim term will not carry its ordinary meaning if the intrinsic evidence shows that the patentee distinguished that term from prior art on the basis of a particular embodiment or described a particular embodiment as important to the invention. *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366-7 (Fed. Cir. 2002); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1325-26, 63 U.S.P.Q.2d 1374, 1380-81 (Fed. Cir. 2002); *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995) ("[t]he prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution"); *see also Spectrum Int'l, Inc. v. Sterilite Corp.*, 164 F.3d 1372, 1378 (Fed. Cir. 1998); *Alpex Computer Corp. v. Nintendo Co.*, 102 F.3d 1214, 1221 (Fed. Cir. 1996) (stating that positions taken before the PTO may bar a later inconsistent position taken on claim construction under § 112, ¶ 6). Yet further, claims cannot be construed in one way to obtain allowance, and then a different way against accused infringers. *Unique Concepts, Inc. v. Brown*, 939 F.2d 1558, 1562 (Fed. Cir. 1991).

Ultimately, through applying the canons of claim construction, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct interpretation." *Renishaw PLC v. Marposs Societa' Per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998). Thus, "[a] claim construction is persuasive, not because it follows a certain rule, but because it defines terms in the context of the whole patent." *Id.*

2. Interpreting the Claims of the '848 Patent

Based on the claims, the specification, and the prosecution history of the '848 patent, a properly informed court would construe the phrase "at least one emulsifying agent comprising an anionic amphiphilic polymer" in accordance with its ordinary and customary meaning, that is, the meaning that the term would have "to a person of ordinary skill in the art in question at the time of the invention . . . ." *Phillips* at 1313. Where, as here, terms have a particular meaning to those of skill in the art, a court may look to "extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* at 1314 (internal quotes omitted).

An "emulsifying agent" or "emulsifier" is:

> a surfactant which when present in small amounts facilitates the formation of an emulsion, or enhances its colloidal stability by decreasing either or both of the rates of aggregation and coalescence.

Definition of "emulsifier", International Union of Pure and Applied Chemistry, "Manual of Symbols and Technology for Physicochemical Quantities and Units", Appendix II, Definitions, Terminology and Symbols in Colloid and Surface Chemistry, PART I, Prepared for Internet Consultation 2001 by L.K. Koopal, accessed February 6, 2006, http://www.iupac.org/reports/2001/colloid_2001/manual_of_s_and_t/node36.html.

Emulsifying agents are therefore surfactants that have the ability to facilitate the formation of an emulsion. Surfactant molecules are characterized, *inter alia*, by an "amphipathic" structure, that is, surfactant molecules

> are composed of groups of opposing solubility tendencies , typically an oil-soluble hydrocarbon chain and a water soluble ionic group. . . . Different designations describe the opposing groups within the surfactant molecules, eg, hydrophobic (water hating) and hydrophilic (water liking) . . . .

Kirk-Othmer Concise Encyclopedia of Chemical Technology, 4th Ed., Vol. 2, Wiley-Interscience (2003), page 1949, column 2 and page 1950, column 1.

"Amphipathic molecules" and "amphiphilic" molecules are both characterized by the presence of hydrophilic groups and hydrophobic groups. The McGraw-Hill Dictionary of Scientific and Technical Terms defines an "amphipathic molecule"

as a "molecule having both hydrophilic and hydrophobic groups". McGraw-Hill Dictionary of Scientific and Technical Terms, 6th Edition (2003), page 89. The term "amphiphilic" is the adjectival form of the noun "amphiphile". The same dictionary identifies "amphiphile" as coming from the field of chemistry and defines it as "[a] molecule which has a polar head attached to a long hydrophobic tail". *Id.* "Amphiphilic" is identified as coming from the field of biochemistry and defined as "[d]escribing a molecule having a polar [hydrophilic] region that is separated from the nonpolar [hydrophobic] region". *Id.*

Surfactant molecules are further classified depending on whether the molecule carries a charge. In "anionic" surfactants the charge is negative, and in "nonionic" surfactants, there is no charge on the molecule. Kirk-Othmer Concise Encyclopedia, page 1950, column 1 and page 1951, column 1. Hydrophilic solubilizing groups in anionic surfactants include carboxylates, sulfonates, sulfates, and phosphates.[1] *Id.* The solubilizing groups in nonionic surfactants include ethylene oxide chains and hydroxyl groups. *Id.* at page 1950, column 1, and page 1952, column 1.[2]

The term "polymer" means a "[s]ubstance made of giant molecules formed by the union of simple molecules (monomers)". McGraw-Hill Dictionary of Scientific and Technical Terms, 6th Edition (2003), page 1635. A molecule that does not contain recurring units derived from monomers is therefore not a polymer.

In view of the foregoing definitions and descriptions, one of ordinary skill in the pharmaceutical formulation arts would understand an "emulsifying agent comprising an anionic amphiphilic polymer" to be a polymeric surfactant capable of stabilizing an emulsion, and having an anionic hydrophilic region, for example a carboxylate group, and a hydrophobic region.

This definition is consistent with use of emulsifiers characterized as "anionic amphiphilic polymers" as used in the claims, specification, and prosecution history of the '848 patent. The specification of the '848 patent states, at column 2, lines 4 to 6, that a stable emulsion is produced by "selecting, as an appropriate

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[1] These groups have both a neutral, protonated form and an anionic, deprotonated form. The fraction of the functional group that exists in the anionic form will depend on the pH of the medium in which the molecule is found. The '848 patent specifies compositions with a pH range of 5 to 7, preferably 5.5 to 6.5. '848 Patent, col. 5, lines 6-9. In this relatively neutral pH range, carboxylic acid groups, for example those in the specific anionic amphiphilic polymers described in the '848 patent, will be substantially present in the anionic form.

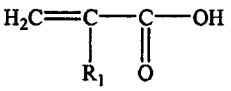
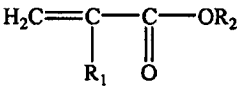
[2] In the relatively neutral pH range specified by the '848 patent, the extent of ionization of these hydroxyl groups is negligible.

emulsifying system, at least one polymeric emulsifier." The specification then describes "anionic amphiphilic polymers" in terms of a specific type of polymer, that is, a polymer based on at least one hydrophilic recurring unit and at least one hydrophobic recurring unit:

> These are, in particular, anionic amphiphilic polymers, more especially those comprising at least one hydrophilic recurring structural unit of the unsaturated olefin carboxylic acid type, and at least one hydrophobic recurring structural unit of the C_{10}-C_{30} alkyl ester type.

'848 Patent, col. 2, lines 10-14.

The structural units can thus be derived from acrylic acid, which provides a hydrophilic recurring structural unit having an anionic group, and a long-chain alkyl acrylate ester, which provides a hydrophobic recurring structural unit.

> According to the invention, acrylic structural units are those of the formula:
>
> 
>
> in which R_1 is H, CH_3 or C_2H_5, namely, acrylic acid, methacrylic acid or ethacrylic acid structural units.
>
> Alkyl acrylate structural units are those of the formula:
>
> 
>
> in which R_1 is H, CH_3 or C_2H_5, namely, acrylate, methacrylate or ethacrylate units, and R_2 is a C_{10}-C_{30}, preferably C_{12}-C_{22}, alkyl radical.

'848 Patent, col. 2, lines 55-33. The carboxylic acid portion of the first structure, the acrylic acids, is shown in the protonated form.

Thus, the only specific embodiment of the "anionic amphiphilic polymer" described in the '848 patent is one in which the polymer includes (1) recurring carboxylic acid-containing units; and (2) recurring C_{10}-C_{30} alkyl ester-containing units. The claims of the '848 patent are also all directed to the foregoing types of anionic amphiphilic polymers. This description and the claims are entirely consistent with the above claim construction wherein an "emulsifying agent comprising an anionic amphiphilic polymer" is interpreted as a polymeric

surfactant capable of stabilizing an emulsion, and having an anionic hydrophilic region, for example a carboxylate group, and a hydrophobic region.

An important question with respect to this definition is the scope of the claim limitation, in particular whether an "emulsifying agent comprising an anionic amphiphilic polymer" could be construed to cover a surfactant containing no carboxylate, sulfonate, sulfate, phosphate, or similar anionic groups. A court would find that such a construction would be improper because it is inconsistent with the plain meaning of the phrase, as it would be understood by one of ordinary skill in the art.

As can be seen from the above description, in particular the excerpt from the Kirk-Othmer Encyclopedia, surfactants are commonly classified as anionic, cationic, nonionic, and amphoteric (containing both positive and negative charges). Kirk-Othmer Concise Encyclopedia, page 1950, column 1. *See also*, "Dispensing of Medication," J. H. Hoover, Ed., Mack Publishing Co. (1976), page 194, column 2 ("The hydrophilic group can be anionic, cationic, or nonionic."). The characterizing feature of an "anionic" surfactant, that is, the feature that distinguishes it from the other types of surfactants, is the presence of an anionic group such as a carboxylate, sulfonate, sulfate, phosphate, or the like. Without one of these anionic groups, a surfactant is not an anionic (nor an amphoteric) surfactant – it is a cationic or nonionic surfactant.

Note in addition that the Kirk-Othmer Concise Encyclopedia specifically names hydroxyl groups as an exemplary solubilizing group in nonionic surfactants. *Id.* at page 1950, column 1, and page 1952, column 1. *See also*, "Dispensing of Medication," page 194, column 2 ("The more lipophilic of [the nonionics] contain a polyhydroxy group such as glycerin or a sorbitan as the hydrophilic group."). The presence of one or more hydroxyl groups in a surfactant is thus clearly insufficient, in and of itself, to render the surfactant an "anionic" surfactant.

One of ordinary skill in the art would therefore understand that an "emulsifying agent comprising an anionic amphiphilic polymer" is not the same as an emulsifying agent comprising a nonionic polymer. One of ordinary skill in the art would further understand that an anionic emulsifying agent must contain at least one anionic group such as carboxylate, sulfonate, sulfate, phosphate, or the like, and that the presence of one or more hydroxyl groups is insufficient, in and of itself, to render the emulsifying agent anionic.

B. Noninfringement Analysis

In the United States, two different types of types of infringement are possible. The first type is "direct infringement", and occurs upon directly practicing the patented invention. The second type, sometimes called "indirect infringement", occurs upon inducing others to directly infringe or contributing to others' direct infringement. 35 U.S.C. § 271 provides in pertinent part as follows:

> (a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.
>
> (b) Whoever actively induces infringement of a patent shall be liable as an infringer.
>
> (c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.

In the United States, a patent may be infringed either literally or under the doctrine of equivalents. Infringement, both literal and under the doctrine of equivalents, is an issue of fact. *SSIH Equip. S.A. v. United States Int'l Trade Comm'n,* 718 F.2d 365, 376, 218 U.S.P.Q. 678, 688 (Fed. Cir. 1983).

1. The Relevant Law of Literal Infringement

As stated above, courts analyze infringement by first, determining the meaning and scope of the asserted patent claims; and secondly, comparing the properly construed claims to the device or method accused of infringing. *Markman v. Westview Instruments Inc.*, 52 F.3d 967, 976, 34 U.S.P.Q.2d 1321, 1326 (Fed. Cir. 1995) *(en banc), aff'd,* 116 S.Ct. 1384, 38 U.S.P.Q.2d 1461 (1996).

To establish literal infringement, every limitation set forth in a claim must be found in an accused product. *Engel Industries, Inc. v. Lockformer Co.*, 96 F.3d

1398, 1405 (Fed. Cir. 1996). "If accused matter falls clearly within the claim, infringement is made out and that is the end of it." *Graver Tank and Mfg Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 607, *reh'g denied,* 340 U.S. 845 (1950).

Further, in the absence of infringement of the independent claims, there can be no infringement of dependent claims. "One who does not infringe an independent claim cannot infringe a claim dependent on (and thus containing all of the limitations of) that claim." *Eltech Systems v. PPG Industries*, 710 F. Supp 622, 634 n.10, 11 U.S.P.Q.2d 1174, 1184 n.10 (W.D. La. 1988), *aff'd*, 903 F.2d 805, 14 U.S.P.Q.2d 1965 (Fed. Cir. 1990).

2. The PROPOSED PRODUCT Does Not Literally Infringe the '848 Patent's Claims

We believe that a properly informed court would find that the PROPOSED PRODUCT would not literally infringe the claims of the '848 patent as construed above.

Claim 1 of the '848 patent requires the presence of an "emulsifying agent comprising an anionic amphiphilic polymer", which, as construed above, means a polymeric surfactant capable of stabilizing an emulsion, and having an anionic hydrophilic region, for example a carboxylate group, and a hydrophobic region. This claim limitation does not include within its scope nonionic surfactants, or surfactants without at least one anionic group such as carboxylate, sulfonate, sulfate, phosphate, or the like.

Two emulsifying agents are present in the PROPOSED PRODUCT, polyoxyethylene 6 isostearate and polyoxyethylene 20 sorbitan monooleate, shown below. Reference to the structures of each of these surfactants shows that neither contains an anionic group such as a carboxylate, sulfonate, sulfate, phosphate, or the like. These surfactants are therefore not anionic, and do not meet the claim limitation requiring an "emulsifying agent comprising an anionic amphiphilic polymer".

Moreover, none of the other components in the PROPOSED PRODUCTS meet the claim limitation requiring an "emulsifying agent comprising an anionic amphiphilic polymer".

Carbomer® 940, a polyacrylic acid poly(acrylic acid), is used to thicken (increase the viscosity) of the PROPOSED PRODUCT. Since Carbomer® 940 acts as a

thickener, rather than an emulsifying agent, it does not satisfy that claim requirement. Note that gelling and/or thickening agents are described in the specification of the '848 patent as a component distinct from the emulsifying agent, and that exemplary gelling and/or thickening agents include various polyacrylic acids. '848 Patent, col. 5, lines 31-42. In addition, Carbomer® 940 is not an "amphiphilic" polymer, because it lacks a hydrophobic group or region. For at least these two reasons, use of Carbomer® 940 in the PROPOSED PRODUCT would not fall within the literal scope of the claim limitation requiring an "emulsifying agent comprising an anionic amphiphilic polymer".

Hydroxypropyl methylcellulose is also used in the PROPOSED PRODUCT as a thickener, and thus does not meet the claim limitation requiring an emulsifier. In addition, since hydroxypropyl methylcellulose does not contain an anionic group such as a carboxylate, sulfonate, sulfate, phosphate, or the like, it is not an anionic polymer. For at least these two reasons, use of hydroxypropyl methylcellulose in the PROPOSED PRODUCT would not fall within the literal scope of the claim limitation requiring an "emulsifying agent comprising an anionic amphiphilic polymer".

None of the other components of the PROPOSED PRODUCTS (clobetasol propionate, mineral oil, propylene glycol, sodium hydroxide, and water) is a polymer, and therefore none of these components meet the claim limitation requiring an "emulsifying agent comprising an anionic amphiphilic polymer".

In sum, the PROPOSED PRODUCT does not contain an "emulsifying agent comprising an amphiphilic polymer", and it therefore would not satisfy at least one very important limitation in the '848 patent claims.

3. The Relevant Law of Infringement Under the Doctrine of Equivalents

Even where no literal infringement exists, a device may infringe a patent under the doctrine of equivalents. *Graver Tank & Mfg. Co., Inc. v. Linde Air Prods. Co.*, 339 U.S. 605, 613 (1950). The doctrine of equivalents permits courts to extend the scope of protection beyond the claim's literal meaning.

However, broad application of the doctrine of equivalents conflicts with the statutory requirement that the claims define the invention. *Warner-Jenkinson Co. v. Hilton Davis Chemical Co.*, 117 S.Ct. 1040, 1049 (1997). The Supreme Court in *Warner-Jenkinson* refused to adopt a particular linguistic framework for

analyzing infringement under the doctrine of equivalents. *Warner-Jenkinson*, 117 S.Ct. at 1054. Instead, the Supreme Court stated that the "essential inquiry" was:

> Does the accused product or process contain elements identical or equivalent to each claimed element of the patented invention? Different linguistic frameworks may be more suitable to different cases, depending on their particular facts. A focus on individual elements and a special vigilance against allowing the concept of equivalence to eliminate completely any such elements should reduce considerably the imprecision of whatever language is used. An analysis of the role played by each element in the context of the specific patent claim will thus inform the inquiry as to whether a substitute element matches the function, way, and result of the claimed element, or whether the substitute element plays a role substantially different from the claimed element. . . . We expect that the Federal Circuit will refine the formulation of the test for equivalence in the orderly course of case-by-case determinations, and we leave such refinement to that court's sound judgment in this area of its special expertise.

Id. at 1054.

The Court of Appeals for the Federal Circuit has also made it clear that the doctrine of equivalents is not intended to be used as a general mechanism for a patentee to expand the scope of a patent's claims. Significant limitations have been placed on the application of the doctrine. First, to infringe under the doctrine of equivalents, a product must include each and every element of a claim or its equivalent. *Warner-Jenkinson*, 117 S. Ct. at 1049 (stating that "[i]t is important to ensure that the application of the doctrine, even as to an individual element, is not allowed such broad play as to effectively eliminate that element in its entirety."). "[T]he doctrine of equivalents is not a license to ignore or erase . . . structural and functional limitations of the claim, limitations on which the public is entitled to rely in avoiding infringement." *Athletic Alternatives, Inc. v. Prince Manu., Inc.*, 73 F.3d 1573, 1582 (Fed. Cir. 1996) (internal quotations omitted).

Thus, if a claim element is totally missing from a device (that is, the claim element is not literally present in the device and an equivalent to the claim element is not present in the device), then there can be no infringement under the doctrine of equivalents as a matter of law. *See Warner-Jenkinson*, 117 S. Ct. at 1049, 1054. This is the so-called "All Elements Rule".

Further, even if equivalence exists, infringement will not be found if subject matter is disclosed but not claimed:

> [W]hen a patent drafter disclosed but declines to claim subject matter . . . this action dedicates that unclaimed subject matter to the public. Application of the doctrine of equivalents to recapture subject matter deliberately left unclaimed would 'conflict with the primacy of the claims in defining the scope of the patentee's exclusive right.'

Johnson & Johnston Assocs. v. R. E. Service Co., 285 F.3d 1046, 1054, 62 U.S.P.Q.2d 1225 (Fed. Cir. 2002) (citations omitted). The only exception to this general rule appears to be when a patentee in fact originally claimed the allegedly equivalent subject matter, but such claim was later invalidated by a court, as in *Graver Tank & MFG. v. Linde Air Prods. Co.*, 336 U.S. 271 (1949).

In addition to these limitations on the doctrine of equivalents, it is well established that where a patentee deliberately claims narrowly in order to distinguish over prior art, the doctrine of equivalents cannot be used to later expand the claims. As stated by the court in *Sextant Avionique S.A. v. Analog Devices Inc.*, 49 U.S.P.Q.2d 1865, 1870:

> Prosecution history estoppel provides a legal limitation on the application of the doctrine of equivalence by excluding from the range of equivalents subject matter surrendered during prosecution of the application for the patent. The estoppel may arise from matter surrendered as a result of amendments to overcome patentability rejections, or as a result of argument to secure allowance of a claim.

It is thus a fundamental principle of patent law that prosecution history estoppel bars recapture of subject matter surrendered during prosecution. *Hilgraeve Corp. v. McAfee Assocs.*, 224 F.3d 1349, 1355, 55 U.S.P.Q.2d (BNA) 1656, 1661 (Fed. Cir. 2000).

The Supreme Court has affirmed that any narrowing amendment to a patent claim made to satisfy any requirements of the Patent Act might give rise to an estoppel. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 122 S.Ct. 1831, 1839 (2002), *subsequent determination, Festo Corp. v. Shoketsu Kinzoku Kogyo*

Kabushiki Co., Ltd., 344 F.3d 1359, 68 U.S.P.Q.2d 1321 (Fed. Cir. 2003*), rehearing en banc denied* (Fed. Cir. 2003). "Estoppel arises when an amendment is made to secure the patent and the amendment narrows the patent's scope." *Id.* at 1840. Thus, if an amendment were "truly cosmetic" it would not narrow the patent's scope or raise an estoppel. The Court of Appeals for the Federal Circuit, in response to the Supreme Court's decision, has provided an analytical framework to aid in the determination of whether, and to what extent, prosecution history estoppel applies, in *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 344 F.3d 1359 (Fed. Cir. 2003).

Explaining that the Warner-Jenkinson and Festo presumptions operate together, the court held that the first question in a prosecution history estoppel inquiry is whether an amendment filed in the PTO has narrowed the literal scope of the claim. If the amendment was not narrowing, then prosecution history estoppel does not apply. *Id.* at 1366.

If the accused infringer establishes that the amendment was a narrowing one, then the second question is whether the reason for the amendment was a substantial one relating to the patentability of the invention. *Id.* When the prosecution history record reveals no reason for the narrowing amendment, it is presumed, under *Warner-Jenkinson*, that the amendment was made for a reason substantially relating to patentability. *Id.* at 1366-67. It is the burden of the patentee to rebut this presumption solely through evidence in the prosecution history record. *Id.* at 1367. If the patentee establishes that the amendment was not for a reason of patentability, then the presumption is rebutted and prosecution history estoppel does not apply. *Id.*

If the patentee is not able to rebut the *Warner-Jenkinson* presumption, the third question addresses the scope of the subject matter surrendered by the narrowing amendment. In accordance with the Supreme Court's decision in *Festo*, it is presumed that the patentee has surrendered all territory between the original claim limitation and the amended claim limitation. *Id.* at 1367. The patentee then bears the burden of showing that a narrowing amendment did not surrender a particular equivalent. *Id.* The patentee may make such a showing one of three ways. The patentee may show (1) that the alleged equivalent would have been unforeseeable at the time of the narrowing amendment; (2) that the rationale underlying the narrowing amendment bore no more than a tangential relation to the equivalent in question, or (3) that there was "some other reason" suggesting that the patentee could not have reasonably been expected to describe the alleged equivalent. *Id.* at 1368, citing *Festo*, 535 U.S. at 740-41, 122 S.Ct. 1831.

The first criterion requires that the patentee show that the alleged equivalent would have been "unforeseeable to one of ordinary skill in the art at the time of the amendment and thus beyond a fair interpretation of what was surrendered". *Id.* at 1369. This criterion presents an objective inquiry, and on its very nature, depends on underlying factual issues relating to, for example, the state of the art and the understanding of a hypothetical person of ordinary skill in the art at the time of the amendment. Therefore, in determining whether an alleged equivalent would have been unforeseeable, a district court may hear expert testimony and consider other extrinsic evidence outside of the procedural history. *Id.*

The second criterion requires that a patentee demonstrate that "the rationale underlying the narrowing amendment [bore] no more than a tangential relation to the equivalent in question." *Id.*, citing *Festo*, 535 U.S. at 740, 122 S.Ct. 1831. As alternately stated, the criterion "asks whether the reason for the narrowing amendment was peripheral, or not directly relevant, to the alleged equivalent." *Id.* The court stated:

> Although we cannot anticipate the instances of mere "tangentialness" that may arise, we can say that an amendment made to avoid prior art that contains the equivalent in question is not tangential; it is central to the allowance of the claim ... Moreover, much like the inquiry into whether a patentee can rebut the *Warner-Jenkinson* presumption that a narrowing amendment was made for a reason of patentability, the inquiry into whether a patentee can rebut the *Festo* presumption under the "tangential" criterion focuses on the patentee's objectively apparent reason for the narrowing amendment. As we have held in the *Warner-Jenkinson* context, that reason should be discernible from the prosecution history record, if the public notice function of a patent and its prosecution history is to have significance .... Thus, whether the patentee has established a merely tangential reason for a narrowing amendment is for the court to determine from the prosecution history record without the introduction of additional evidence, except when necessary, testimony from those skilled in the art as to the interpretation of that record.

Id. at 1369-1370. At least one case has directly addressed whether an amendment was merely tangential to the equivalent in question, *Insituform Technologies, Inc. v. CAT Contracting, Inc.*, 385 F.3d 1360, 1367 (Fed.Cir. 2004). In this case, the

question was whether a process using multiple cups to establish a vacuum infringed a claim using one cup, when the original claim had not limited the number of cups that could be used. The patentee successfully rebutted the presumption that the equivalent in question, multiple cups, had not been surrendered because the prosecution history showed that the limitation requiring one cup was added to overcome art that was directed to where the vacuum was placed, rather than the number of cups. *Id.* at 8-10.

The third criterion requires a patentee to establish "some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question." *Id.* at 1370. As stated by the court, the category, "while vague, must be a narrow one; it is available in order not to totally foreclose a patentee from relying on reasons, other than unforseeability and tangentialness, to show that it did not surrender the alleged equivalent." *Id.* It may be satisfied when "there was some reason, such as the shortcomings of language, why the patentee was prevented from describing the alleged equivalent when it narrowed the claim." *Id.* This criterion should be limited to prosecution history record when possible. *Id.*

In addition, Federal Circuit has reaffirmed the doctrine of argument-based estoppel, by reiterating that arguments made voluntarily during prosecution may give rise to prosecution history estoppel if they evidence a surrender of subject matter. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.,* 234 F.3d 558, 589 (Fed. Cir. 2000); *KCJ Corp. v. Kinetic Concepts, Inc.,* 223 F. 3d 1351, 1359-60 (Fed. Cir. 2000) (KCJ's statements made during prosecution reflect a clear and unmistakable surrender of subject matter and cannot be recaptured through the doctrine of equivalents). Thus, clear assertions made during prosecution in support of patentability create an estoppel whether or not actually required to secure allowance of the case. *Southwall Techs. Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1583 (Fed. Cir. 1995). Furthermore, patent holders are prevented from asserting infringement under the doctrine of equivalents for a feature that was argued as being important for patentability. *Texas Instruments, Inc. v. United States Int'l Trade Comm'n,* 988 F.2d 1165, 1174 (Fed. Cir. 1993). Such a result is also favored by a strong trend in the recent decisions by the U.S. courts that have favored the public notice aspect of patent claims (based on the intrinsic evidence including the statements made during prosecution) over any expansion of a patentee's rights under the doctrine of equivalents. *See, e.g., Festo,* 234 F.3d 558, 574-78 (Fed. Cir. 2000).

The final limitation on the doctrine of equivalents is the prior art. Determining whether an allegedly infringing product is covered by the prior art (and thus excluded from a claim's range of equivalents) is governed by *Wilson Sporting Goods Co. v. David Geoffrey & Associates*, 904 F.2d 677, 14 U.S.P.Q.2d 1942 (Fed. Cir. 1990), *cert. denied*, 111 S. Ct. 537 (1990).

Beyond the above limitations, various Federal Circuit decisions in recent years have shown a trend toward limiting the application of the doctrine of equivalents to find infringement. *See generally, Sage Prods., Inc. v. Devon Indus., Inc.*, 126 F.3d 1420 (Fed. Cir. 1997); *Vehicular Tech. Corp. v. Titan Wheel Int'l, Inc.*, 141 F.3d 1084 (Fed. Cir. 1998); *Dawn Equip. Co. v. Kentucky Farms Inc.*, 140 F.3d 1009 (Fed. Cir. 1998). In *Sage Products*, the Court made the following comments regarding the doctrine:

> [The patentee] left the PTO with manifestly limited claims that it now seeks to expand through the doctrine of equivalents. However, as between the patentee who had a clear opportunity to negotiate broader claims but did not do so, and the public at large, it is the patentee who must bear the cost of its failure to seek protection for this foreseeable alteration of its claimed structure. . . . . Given a choice of imposing the higher costs of careful prosecution on patentees, or imposing the costs of foreclosed business activity on the public at large, this court believes the costs are properly imposed on the group best positioned to determine whether or not a particular invention warrants investment at a higher level, that is, the patentees.

Id. at 1425.

In *Sage Products*, the Court concluded that because the claims at issue contained "clear structural limitations" on which the public is entitled to rely, and because those limitations were missing from the accused infringing device, there was no infringement, either literally or under the doctrine of equivalents. *Id.*

4. The PROPOSED PRODUCT Does Not Infringe the '848 Patent's Claims Under the Doctrine of Equivalents

The doctrine of equivalents was judicially created to prevent "pirating" of another's invention by avoiding the literal claim language. It is intended to allow a patentee to encompass "insubstantial changes" from a claimed invention within the scope of the patent. Here, howevever, a properly informed court would find that the doctrine of equivalents limits the scope of equivalents of the claim limitation requiring an "emulsifying agent comprising an anionic amphiphilic polymer".

The first step of the *Festo* analysis asks whether an amendment filed in the PTO has narrowed the literal scope of the claim. Here, the answer is yes. As filed, claim 1 of the '054 application recited "at least one emulsifying agent" without any limitation on the type or structure of the emulsifying agent. '054 Application, page 14. In the Amendment dated 3/15/99, the Applicants amended claim 1 to add the limitation that the emulsifying agent "consist[s] essentially of an anionic amphiphilic polymer". Claim 1 was subsequently amended to replace "consisting essentially of" with "comprising". Preliminary Amendment dated 1/19/00. Nonetheless, the literal scope of claim 1 was still narrowed relative to the claim as originally filed, because the group of emulsifying agents was limited, from any emulsifying agent to anionic amphiphilic polymers. The prosecution history of the '848 patent therefore includes amendments narrowing the literal scope of the emulsifying agent in claim 1, satisfying the first step of the *Festo* analysis.

The second question in *Festo* analysis is whether the reason for the amendment was a substantial one relating to the patentability of the invention. Again, the answer is yes. The limitation requiring the emulsifying agent to be an anionic amphiphilic polymer was added in response to a rejection of all claims as anticipated by or obvious over WO 94/17830. In the rejection, the examiner stated that he "finds all the components as claimed are present and known in the prior art . . ." 12/15/98 Office Action, page 2, last paragraph. Applicants responded by amending claim 1 to limit the emulsifying agent to "consisting essentially of an anionic amphiphilic polymer" and arguing that WO 94/17830 "fails to teach or suggest a composition as claimed, containing an emulsifying agent which consist *[sic]* essentially of an anionic amphiphilic polymer." 3/15/99 Amendment, page 5, last paragraph; *see also*, 9/7/99 Amendment, page 6, last paragraph. Since claim 1 was amended to distinguish the emulsifying agent as originally claimed from the emulsifying agents of WO 94/17830, the amendment was a substantial one relating to the patentability of the invention.

As explained above, if a narrowing amendment is made, and that amendment is a substantial one relating to patentability, it is presumed that the patentee has surrendered all territory between the original claim limitation (i.e., "at least one emulsifying agent") and the amended claim limitation (i.e., "at least one emulsifying agent comprising an anionic amphiphilic polymer"). *Festo*, 344 F.3d at 1367. The patentee then bears the burden of showing that a narrowing amendment did not surrender a particular equivalent. *Id.* The patentee may make such a showing one of three ways. The patentee may show (1) that the alleged equivalent would have been unforeseeable at the time of the narrowing amendment; (2) that the rationale underlying the narrowing amendment bore no more than a tangential relation to the equivalent in question, or (3) that there was "some other reason" suggesting that the patentee could not have reasonably been expected to describe the alleged equivalent. *Id.* at 1368, citing *Festo*, 535 U.S. at 740-41, 122 S.Ct. 1831. Here, there is no evidence that the patentee will be able to make any of the foregoing showings.

First, the patentee cannot successfully argue that the alleged equivalent (i.e., use of polyoxyethylene 6 isostearate and polyoxyethylene 20 sorbitan monooleate as emulsifying agents) was unforeseeable, because the '848 patent itself discloses such materials as "coemulsifying agents". In particular, the coemulsifiers listed in the '848 patent include "PEG-6 isostearate marketed under the trademark OLEPAL ISOSTEARIQUE by GATTEFOSSE" and "the esters of sorbitol and oleic acid such as the polysorbates marketed under the trademark TWEEN by ICI". '848 Patent, col. 5, lines 10-30. TWEEN 80 is known to be equivalent to the polysorbate 80 used in the PROPOSED PRODUCT. Handbook of Pharmaceutical Excipients, entry for Polyoxyethylene Sorbitan Fatty Acid Esters, p. 479. Thus, because the types of emulsifying agents used in the PROPOSED PRODUCT are not only known, but disclosed in the specification of the '848 patent, the patentee cannot argue that their use would have been unforeseeable at the time of the narrowing amendment.

Second, the patentee cannot successfully argue that the rationale underlying the narrowing amendment bore no more than a tangential relation to the equivalent in question. The amendment in question – requiring the emulsifying agent to be an "anionic amphiphilic polymer" – was made in response to an art-based rejection under 35 U.S.C. § 102 and/or § 103 over WO 94/17830, concurrently with the argument that WO 94/17830 did not teach an anionic amphiphilic polymer as an emulsifying agent. 3/15/99 Amendment, page 5, last paragraph; *see also*, 9/7/99 Amendment, page 6, last paragraph. The amendment in question is therefore

central to the alleged equivalents, which are emulsifying agents that are not anionic amphiphilic polymers.

Third, there is no basis for an assertion that there was "some other reason" suggesting that the patentee could not have reasonably been expected to describe the alleged equivalent. Here, patentee did describe the alleged equivalent as an optional "coemulsifier". As noted above, the '848 patent's coemulsifiers include "PEG-6 isostearate marketed under the trademark OLEPAL ISOSTEARIQUE by GATTEFOSSE" and "the esters of sorbitol and oleic acid such as the polysorbates marketed under the trademark TWEEN by ICI". '848 Patent, col. 5, lines 10-30. TWEEN 80 is known to be equivalent to the polysorbate 80 used in the PROPOSED PRODUCT. Handbook of Pharmaceutical Excipients, entry for Polyoxyethylene Sorbitan Fatty Acid Esters, p. 479. Thus, since patentee described the alleged equivalent in the '848 patent's written description, it will be difficult for the patentee to argue that there was "some other reason" that patentee could not have reasonably been expected to describe the alleged equivalent.

In sum, there is no rationale that the patentee could use to rebut the presumption that the patentee has surrendered all territory between the original claim limitation. The patentee therefore cannot expand the literal scope of the limitation requiring an "emulsifying agent comprising an anionic amphiphilic polymer" via the doctrine of equivalents. Accordingly, the doctrine of equivalents cannot be used to expand the term "anionic amphiphilic polymer" to encompass any of the components of the PROPOSED PRODUCT.

IV. CONCLUSION

For at least the reasons stated above, Actavis' activity in making, using, and selling the PROPOSED PRODUCT will not infringe the '848 patent's claims either literally or under the doctrine of equivalents.

Sincerely,

Terri Nataline, Esq.
Director, Intellectual Property
Actavis Mid Atlantic LLC

OFFER OF CONFIDENTIAL ACCESS AND CONFIDENTIALITY AGREEMENT

Pursuant to 35 U.S.C. § 355(j)(2)(B), Actavis Mid Atlantic LLC. ("Actavis"), a subsidiary of Actavis Group, has provided notice (the "Notice Letter") to the undersigned that it intends to market a drug product under Abbreviated New Drug Application ("ANDA") number 78-223 before the expiration date of U.S. Patent No. 6,106,848. Such notice sets forth, among other things, a detailed statement of the factual and legal basis of Actavis' opinion that the claims of U.S. Patent No.6,106,848 are invalid and/or will not be infringed by the commercial manufacture, use or sale of the proposed drug product. For the sole purpose of allowing the undersigned to determine whether an action referred to in 21 U.S.C. § 355(j)(5)(B)(iii) should be brought, Actavis hereby offers to provide confidential access to ANDA No. 78-223, subject to the restrictions set forth herein. By requesting such confidential access and acknowledging this Offer of Confidential Access and Confidentiality Agreement ("Agreement"), the undersigned hereby agrees as follows:

(1) This Agreement shall apply to all information, documents and things relating to ANDA No. 78-223 made available or otherwise disclosed by Actavis or its counsel to the undersigned or its counsel in connection with the Notice Letter. Such information and materials are hereinafter collectively referred to as "Confidential Information."

(2) Any copy, summary, extract, description or other document containing Confidential Information shall be subject to the terms of this Agreement to the same extent as the information or document from which such copy, summary, extract, description or other document was made.

(3) Access to Confidential Information shall be limited solely to:

(a) partners and associate attorneys and secretarial, paralegal and staff personnel of outside attorneys for the undersigned;

(b) a single in-house attorney of the undersigned, provided that such in-house attorney (i) makes no further disclosure of all or part of the Confidential Information, (ii) is specifically identified in writing prior to such disclosure and (iii) executes an acknowledgement of the Agreement in the form attached hereto as Exhibit A; and

(c) any outside copying service, provided that before any such disclosure is made the authorized representative of said copying service executes an acknowledgement of the Agreement in the form attached hereto as Exhibit A.

(4) No person to whom any Confidential Information is disclosed shall make any further disclosure thereof.

(5) No person to whom any Confidential Information is disclosed shall use such information except for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the Notice Letter.

(6) Nothing contained herein shall be construed to restrict disclosure and use of documents, information or things to any person who in the course of his business duties had previously prepared, lawfully received or had rightful access to such documents, information or things.

(7) Nothing contained herein shall obligate Actavis to disclose any information to the undersigned relating to ANDA No. 78-223 or any other subject matter whatsoever.

(8) Unless otherwise agreed in writing, Confidential Information, all copies thereof, and any extracts, descriptions or summaries thereof, are to be destroyed or returned to Actavis immediately following the passage of 45 days after the undersigned's receipt of the Notice Letter.

(9) Nothing herein shall prevent disclosure beyond the terms of this Agreement if Actavis agrees to such disclosure in writing or as required by law, in which case the undersigned shall provide Actavis with prior notice sufficient to seek a protective order.

(10) Actavis shall not be deemed to have waived the attorney/client privilege or attorney work product privilege by virtue of this Agreement or the disclosure of any Confidential Information hereunder.

(11) This Agreement shall be governed and construed in accordance with the laws of the State of New York without regard to its conflicts-of-law rules.

ACCORDINGLY, intending to be bound by the terms of this Agreement and agreeing that it is in its respective commercial interest to be so bound, the undersigned does hereby acknowledge its agreement by its signature below.

Dated: _____ Company: _____

By: _____

Name: _____

Its: _____

EXHIBIT A

AGREEMENT CONCERNING MATERIAL
COVERED BY A CONFIDENTIALITY AGREEMENT

The undersigned hereby acknowledges that he or she has received and read the Offer of Confidential Access and Confidentiality Agreement (the "Agreement") executed by _____ on _____. The undersigned agrees to be bound by such terms, and agrees to submit to the jurisdiction of the United States District Court for the Southern District of New York for the purpose of enforcing the terms of the Agreement.

Dated: _____

_____
(Signature)

ORIGINAL

JS 44 (Rev. 11/04)

CIVIL COVER SHEET

The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. (SEE INSTRUCTIONS ON THE REVERSE OF THE FORM.)

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CLERK OF COURT

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JUN 30 2006

CLERK, U.S. DISTRICT COURT
NORTHERN DISTRICT OF TEXAS

I. (a) PLAINTIFFS
Galderma Laboratories, L.P. and Galderma, S.A.

DEFENDANTS
Actavis Mid-Atlantic, L.L.C.

(b) County of Residence of First Listed Plaintiff Tarrant County, TX
(EXCEPT IN U.S. PLAINTIFF CASES)

County of Residence of First Listed Defendant Union County, NJ
(IN U.S. PLAINTIFF CASES ONLY)
NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE LAND INVOLVED.

(c) Attorney's (Firm Name, Address, and Telephone Number)
Munck Butrus, P.C., 13155 Noel Rd., Ste. 900, Dallas, TX 75240
(972) 628-3600, (see attachment)

Attorneys (If Known)

3-06CV1176-N

II. BASIS OF JURISDICTION (Place an "X" in One Box Only)

- ☐ 1 U.S. Government Plaintiff
- ☒ 3 Federal Question (U.S. Government Not a Party)
- ☐ 2 U.S. Government Defendant
- ☐ 4 Diversity (Indicate Citizenship of Parties in Item III)

III. CITIZENSHIP OF PRINCIPAL PARTIES (Place an "X" in One Box for Plaintiff and One Box for Defendant)
(For Diversity Cases Only)

	PTF	DEF		PTF	DEF
Citizen of This State	☐ 1	☐ 1	Incorporated *or* Principal Place of Business In This State	☐ 4	☐ 4
Citizen of Another State	☐ 2	☐ 2	Incorporated *and* Principal Place of Business In Another State	☐ 5	☐ 5
Citizen or Subject of a Foreign Country	☐ 3	☐ 3	Foreign Nation	☐ 6	☐ 6

IV. NATURE OF SUIT (Place an "X" in One Box Only)

CONTRACT	TORTS		FORFEITURE/PENALTY	BANKRUPTCY	OTHER STATUTES
☐ 110 Insurance	PERSONAL INJURY	PERSONAL INJURY	☐ 610 Agriculture	☐ 422 Appeal 28 USC 158	☐ 400 State Reapportionment
☐ 120 Marine	☐ 310 Airplane	☐ 362 Personal Injury - Med Malpractice	☐ 620 Other Food & Drug	☐ 423 Withdrawal 28 USC 157	☐ 410 Antitrust
☐ 130 Miller Act	☐ 315 Airplane Product Liability	☐ 365 Personal Injury - Product Liability	☐ 625 Drug Related Seizure of Property 21 USC 881		☐ 430 Banks and Banking
☐ 140 Negotiable Instrument	☐ 320 Assault, Libel & Slander	☐ 368 Asbestos Personal Injury Product Liability	☐ 630 Liquor Laws	PROPERTY RIGHTS	☐ 450 Commerce
☐ 150 Recovery of Overpayment & Enforcement of Judgment	☐ 330 Federal Employers' Liability	PERSONAL PROPERTY	☐ 640 R.R. & Truck	☐ 820 Copyrights	☐ 460 Deportation
☐ 151 Medicare Act	☐ 340 Marine	☐ 370 Other Fraud	☐ 650 Airline Regs.	☒ 830 Patent	☐ 470 Racketeer Influenced and Corrupt Organizations
☐ 152 Recovery of Defaulted Student Loans (Excl. Veterans)	☐ 345 Marine Product Liability	☐ 371 Truth in Lending	☐ 660 Occupational Safety/Health	☐ 840 Trademark	☐ 480 Consumer Credit
☐ 153 Recovery of Overpayment of Veteran's Benefits	☐ 350 Motor Vehicle	☐ 380 Other Personal Property Damage	☐ 690 Other		☐ 490 Cable/Sat TV
☐ 160 Stockholders' Suits	☐ 355 Motor Vehicle Product Liability	☐ 385 Property Damage Product Liability	LABOR	SOCIAL SECURITY	☐ 810 Selective Service
☐ 190 Other Contract	☐ 360 Other Personal Injury		☐ 710 Fair Labor Standards Act	☐ 861 HIA (1395ff)	☐ 850 Securities/Commodities/ Exchange
☐ 195 Contract Product Liability			☐ 720 Labor/Mgmt. Relations	☐ 862 Black Lung (923)	☐ 875 Customer Challenge 12 USC 3410
☐ 196 Franchise			☐ 730 Labor/Mgmt. Reporting & Disclosure Act	☐ 863 DIWC/DIWW (405(g))	☐ 890 Other Statutory Actions
REAL PROPERTY	CIVIL RIGHTS	PRISONER PETITIONS	☐ 740 Railway Labor Act	☐ 864 SSID Title XVI	☐ 891 Agricultural Acts
☐ 210 Land Condemnation	☐ 441 Voting	☐ 510 Motions to Vacate Sentence	☐ 790 Other Labor Litigation	☐ 865 RSI (405(g))	☐ 892 Economic Stabilization Act
☐ 220 Foreclosure	☐ 442 Employment	Habeas Corpus:	☐ 791 Empl. Ret. Inc. Security Act	FEDERAL TAX SUITS	☐ 893 Environmental Matters
☐ 230 Rent Lease & Ejectment	☐ 443 Housing/ Accommodations	☐ 530 General		☐ 870 Taxes (U.S. Plaintiff or Defendant)	☐ 894 Energy Allocation Act
☐ 240 Torts to Land	☐ 444 Welfare	☐ 535 Death Penalty		☐ 871 IRS—Third Party 26 USC 7609	☐ 895 Freedom of Information Act
☐ 245 Tort Product Liability	☐ 445 Amer. w/Disabilities - Employment	☐ 540 Mandamus & Other			☐ 900 Appeal of Fee Determination Under Equal Access to Justice
☐ 290 All Other Real Property	☐ 446 Amer. w/Disabilities - Other	☐ 550 Civil Rights			☐ 950 Constitutionality of State Statutes
	☐ 440 Other Civil Rights	☐ 555 Prison Condition			

V. ORIGIN (Place an "X" in One Box Only)

☒ 1 Original Proceeding ☐ 2 Removed from State Court ☐ 3 Remanded from Appellate Court ☐ 4 Reinstated or Reopened ☐ 5 Transferred from another district (specify) ☐ 6 Multidistrict Litigation ☐ 7 Appeal to District Judge from Magistrate Judgment

Cite the U.S. Civil Statute under which you are filing **(Do not cite jurisdictional statutes unless diversity)**:

VI. CAUSE OF ACTION

Brief description of cause: Patent infringement action.

VII. REQUESTED IN COMPLAINT:

☐ CHECK IF THIS IS A CLASS ACTION UNDER F.R.C.P. 23

DEMAND $

CHECK YES only if demanded in complaint:
JURY DEMAND: ☒ Yes ☐ No

VIII. RELATED CASE(S) IF ANY

(See instructions): JUDGE _____ DOCKET NUMBER _____

DATE
June 30, 2006

SIGNATURE OF ATTORNEY OF RECORD

FOR OFFICE USE ONLY

RECEIPT # _____ AMOUNT _____ APPLYING IFP _____ JUDGE _____ MAG. JUDGE _____

JS 44 Reverse (Rev. 11/04)

INSTRUCTIONS FOR ATTORNEYS COMPLETING CIVIL COVER SHEET FORM JS 44

Authority For Civil Cover Sheet

The JS 44 civil cover sheet and the information contained herein neither replaces nor supplements the filings and service of pleading or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. Consequently, a civil cover sheet is submitted to the Clerk of Court for each civil complaint filed. The attorney filing a case should complete the form as follows:

I. (a) Plaintiffs-Defendants. Enter names (last, first, middle initial) of plaintiff and defendant. If the plaintiff or defendant is a government agency, use only the full name or standard abbreviations. If the plaintiff or defendant is an official within a government agency, identify first the agency and then the official, giving both name and title.

(b) County of Residence. For each civil case filed, except U.S. plaintiff cases, enter the name of the county where the first listed plaintiff resides at the time of filing. In U.S. plaintiff cases, enter the name of the county in which the first listed defendant resides at the time of filing. (NOTE: In land condemnation cases, the county of residence of the "defendant" is the location of the tract of land involved.)

(c) Attorneys. Enter the firm name, address, telephone number, and attorney of record. If there are several attorneys, list them on an attachment, noting in this section "(see attachment)".

II. Jurisdiction. The basis of jurisdiction is set forth under Rule 8(a), F.R.C.P., which requires that jurisdictions be shown in pleadings. Place an "X" in one of the boxes. If there is more than one basis of jurisdiction, precedence is given in the order shown below.

United States plaintiff. (1) Jurisdiction based on 28 U.S.C. 1345 and 1348. Suits by agencies and officers of the United States are included here.

United States defendant. (2) When the plaintiff is suing the United States, its officers or agencies, place an "X" in this box.

Federal question. (3) This refers to suits under 28 U.S.C. 1331, where jurisdiction arises under the Constitution of the United States, an amendment to the Constitution, an act of Congress or a treaty of the United States. In cases where the U.S. is a party, the U.S. plaintiff or defendant code takes precedence, and box 1 or 2 should be marked.

Diversity of citizenship. (4) This refers to suits under 28 U.S.C. 1332, where parties are citizens of different states. When Box 4 is checked, the citizenship of the different parties must be checked. (See Section III below; federal question actions take precedence over diversity cases.)

III. Residence (citizenship) of Principal Parties. This section of the JS 44 is to be completed if diversity of citizenship was indicated above. Mark this section for each principal party.

IV. Nature of Suit. Place an "X" in the appropriate box. If the nature of suit cannot be determined, be sure the cause of action, in Section VI below, is sufficient to enable the deputy clerk or the statistical clerks in the Administrative Office to determine the nature of suit. If the cause fits more than one nature of suit, select the most definitive.

V. Origin. Place an "X" in one of the seven boxes.

Original Proceedings. (1) Cases which originate in the United States district courts.

Removed from State Court. (2) Proceedings initiated in state courts may be removed to the district courts under Title 28 U.S.C., Section 1441. When the petition for removal is granted, check this box.

Remanded from Appellate Court. (3) Check this box for cases remanded to the district court for further action. Use the date of remand as the filing date.

Reinstated or Reopened. (4) Check this box for cases reinstated or reopened in the district court. Use the reopening date as the filing date.

Transferred from Another District. (5) For cases transferred under Title 28 U.S.C. Section 1404(a). Do not use this for within district transfers or multidistrict litigation transfers.

Multidistrict Litigation. (6) Check this box when a multidistrict case is transferred into the district under authority of Title 28 U.S.C. Section 1407. When this box is checked, do not check (5) above.

Appeal to District Judge from Magistrate Judgment. (7) Check this box for an appeal from a magistrate judge's decision.

VI. Cause of Action. Report the civil statute directly related to the cause of action and give a brief description of the cause. **Do not cite jurisdictional statutes unless diversity.** Example: U.S. Civil Statute: 47 USC 553
Brief Description: Unauthorized reception of cable service

VII. Requested in Complaint. Class Action. Place an "X" in this box if you are filing a class action under Rule 23, F.R.Cv.P.

Demand. In this space enter the dollar amount (in thousands of dollars) being demanded or indicate other demand such as a preliminary injunction.

Jury Demand. Check the appropriate box to indicate whether or not a jury is being demanded.

VIII. Related Cases. This section of the JS 44 is used to reference related pending cases if any. If there are related pending cases, insert the docket numbers and the corresponding judge names for such cases.

Date and Attorney Signature. Date and sign the civil cover sheet.